Number (%) of Patients With Specific Clinical Adverse Experiences (Incidence >0% in One or More Treatment Groups) by System Organ Class – Open-Label Post Virologic Failure (Protocols 005, 018, and 019) - *Cumulative Data*

	MK-0518 (N = 223)	
	n	(%)
Musculoskeletal And Connective Tissue Disorders	28	(12.6)
Osteoarthritis	1	(0.4)
Osteonecrosis	1	(0.4)
Osteoporosis	1	(0.4)
Pain In Extremity	2	(0.9)
Synovial Cyst	1	(0.4)
Tendon Disorder	1	(0.4)
Tendonitis	3	(1.3)
Neoplasms Benign, Malignant And Unspecified (Incl Cysts And Polyps)	6	(2.7)
Anal Cancer	1	(0.4)
Basal Cell Carcinoma	1	(0.4)
Hodgkin's Disease	2	(0.9)
Skin Papilloma	2	(0.9)
Squamous Cell Carcinoma	1	(0.4)
Nervous System Disorders	24	(10.8)
Balance Disorder	1	(0.4)
Convulsions Local	1	(0.4)
Disturbance In Attention	1	(0.4)
Dizziness	3	(1.3)
Dysgeusia	1	(0.4)
Facial Neuralgia	1	(0.4)
Headache	8	(3.6)

Number (%) of Patients With Specific Clinical Adverse Experiences (Incidence >0% in One or More Treatment Groups) by System Organ Class – Open-Label Post Virologic Failure (Protocols 005, 018, and 019) - *Cumulative Data*

	MK-0518 (N = 223)	
	n	(%)
Nervous System Disorders	24	(10.8)
Hypoaesthesia	2	(0.9)
Hypogeusia	1	(0.4)
Hyposmia	1	(0.4)
Memory Impairment	2	(0.9)
Neuropathy Peripheral	1	(0.4)
Sciatica	2	(0.9)
Somnolence	3	(1.3)
Syncope	1	(0.4)
Psychiatric Disorders	18	(8.1)
Anxiety	2	(0.9)
Depression	6	(2.7)
Euphoric Mood	1	(0.4)
Hallucination	1	(0.4)
Insomnia	6	(2.7)
Libido Decreased	1	(0.4)
Panic Attack	1	(0.4)
Post-Traumatic Stress Disorder	1	(0.4)
Sleep Disorder	1	(0.4)
Sopor	1	(0.4)
Suicidal Ideation	1	(0.4)
Renal And Urinary Disorders	7	(3.1)

Number (%) of Patients With Specific Clinical Adverse Experiences (Incidence >0% in One or More Treatment Groups) by System Organ Class – Open-Label Post Virologic Failure (Protocols 005, 018, and 019) - *Cumulative Data*

	MK-0518 (N = 223)	
	n	(%)
Renal And Urinary Disorders	7	(3.1)
Nephrolithiasis	1	(0.4)
Polyuria	1	(0.4)
Proteinuria	1	(0.4)
Renal Colic	1	(0.4)
Renal Failure	2	(0.9)
Renal Failure Acute	1	(0.4)
Reproductive System And Breast Disorders	10	(4.5)
Benign Prostatic Hyperplasia	1	(0.4)
Breast Pain	1	(0.4)
Epididymitis	1	(0.4)
Erectile Dysfunction	4	(1.8)
Genital Lesion	1	(0.4)
Pelvic Pain	1	(0.4)
Scrotal Erythema	1	(0.4)
Respiratory, Thoracic And Mediastinal Disorders	23	(10.3)
Asthma	1	(0.4)
Bronchial Hyperreactivity	1	(0.4)
Cough	9	(4.0)
Dyspnoea	1	(0.4)
Dyspnoea Exertional	1	(0.4)
Hyperventilation	1	(0.4)

Number (%) of Patients With Specific Clinical Adverse Experiences (Incidence >0% in One or More Treatment Groups) by System Organ Class – Open-Label Post Virologic Failure (Protocols 005, 018, and 019) - *Cumulative Data*

	MK-0518 (N = 223)	
	n	(%)
Respiratory, Thoracic And Mediastinal Disorders	23	(10.3)
Lung Disorder	1	(0.4)
Nasal Congestion	2	(0.9)
Pleural Effusion	1	(0.4)
Productive Cough	1	(0.4)
Pulmonary Congestion	1	(0.4)
Rhinitis Allergic	4	(1.8)
Rhinitis Seasonal	1	(0.4)
Sinus Congestion	1	(0.4)
Sleep Apnoea Syndrome	2	(0.9)
Skin And Subcutaneous Tissue Disorders	34	(15.2)
Acne	1	(0.4)
Dermatitis	1	(0.4)
Dermatitis Contact	1	(0.4)
Drug Eruption	1	(0.4)
Dyshidrosis	1	(0.4)
Eczema	2	(0.9)
Erythema	2	(0.9)
Henoch-Schonlein Purpura	1	(0.4)
Hyperkeratosis	1	(0.4)
Lipodystrophy Acquired	1	(0.4)
Night Sweats	1	(0.4)

Number (%) of Patients With Specific Clinical Adverse Experiences (Incidence >0% in One or More Treatment Groups) by System Organ Class – Open-Label Post Virologic Failure (Protocols 005, 018, and 019) - *Cumulative Data*

	MK-0518 (N = 223)	
	n	(%)
Skin And Subcutaneous Tissue Disorders	34	(15.2)
Pruritus	3	(1.3)
Rash	10	(4.5)
Rash Maculo-Papular	1	(0.4)
Rash Papular	2	(0.9)
Rash Pruritic	1	(0.4)
Seborrhoea	1	(0.4)
Skin Discolouration	1	(0.4)
Skin Fissures	1	(0.4)
Skin Hyperpigmentation	1	(0.4)
Skin Lesion	2	(0.9)
Skin Ulcer	1	(0.4)
Subcutaneous Nodule	5	(2.2)
Vascular Disorders	6	(2.7)
Haematoma	1	(0.4)
Hypertension	3	(1.3)
Thrombophlebitis	1	(0.4)
Varicose Vein	1	(0.4)

Although a patient may have had two or more clinical adverse experiences, the patient is counted only once within a category. The same patient may appear in different categories.

Note: MK-0518 and Placebo were administered with Optimized Background Therapy (OBT).

Adverse experience terms are from MedDRA Version 9.1.

[Ref. 5.3.5.1: P005-Define, P018-Define, P019-Define]

Appendix 2.7.4: 30

Number (%) of Patients With Specific Clinical Adverse Experiences (Incidence >0% in One or More Treatment Groups) by System Organ Class – Open-Label Post Virologic Failure (Protocols 005, 018, and 019) - *Original Application*

	MK-0518 (N = 177)	
	n	(%)
Patients With One Or More Adverse Experiences	100	(56.5)
Patients With No Adverse Experience	77	(43.5)
Blood And Lymphatic System Disorders	7	(4.0)
Anaemia	2	(1.1)
Bone Marrow Toxicity	1	(0.6)
Lymphadenopathy	4	(2.3)
Neutropenia	1	(0.6)
Cardiac Disorders	2	(1.1)
Angina Unstable	1	(0.6)
Palpitations	1	(0.6)
Eye Disorders	4	(2.3)
Conjunctival Haemorrhage	1	(0.6)
Eye Oedema	1	(0.6)
Eyelid Oedema	1	(0.6)
Lacrimation Increased	2	(1.1)
Photophobia	1	(0.6)
Gastrointestinal Disorders	33	(18.6)
Abdominal Distension	1	(0.6)
Abdominal Pain	4	(2.3)
Abdominal Pain Upper	1	(0.6)
Bowel Sounds Abnormal	1	(0.6)
Constipation	3	(1.7)

Number (%) of Patients With Specific Clinical Adverse Experiences (Incidence >0% in One or More Treatment Groups) by System Organ Class – Open-Label Post Virologic Failure (Protocols 005, 018, and 019) - *Original Application*

	MK-0518 (N = 177)	
	n	(%)
Gastrointestinal Disorders	33	(18.6)
Dental Caries	3	(1.7)
Diarrhoea	7	(4.0)
Dry Mouth	2	(1.1)
Duodenitis	1	(0.6)
Dyspepsia	3	(1.7)
Faecal Incontinence	1	(0.6)
Flatulence	1	(0.6)
Food Poisoning	1	(0.6)
Gingival Disorder	1	(0.6)
Gingivitis	4	(2.3)
Haematemesis	1	(0.6)
Lip Ulceration	1	(0.6)
Nausea	6	(3.4)
Oesophagitis	1	(0.6)
Proctitis	1	(0.6)
Salivary Hypersecretion	1	(0.6)
Tongue Eruption	1	(0.6)
Vomiting	5	(2.8)
General Disorders And Administration Site Conditions	25	(14.1)
Asthenia	1	(0.6)
Chest Pain	2	(1.1)
Chills	2	(1.1)

Number (%) of Patients With Specific Clinical Adverse Experiences (Incidence >0% in One or More Treatment Groups) by System Organ Class – Open-Label Post Virologic Failure (Protocols 005, 018, and 019) - *Original Application*

	MK-0518 (N = 177)	
	n	(%)
General Disorders And Administration Site Conditions	25	(14.1)
Drug Intolerance	2	(1.1)
Fatigue	6	(3.4)
Feeling Hot	1	(0.6)
Influenza Like Illness	2	(1.1)
Injection Site Reaction	3	(1.7)
Nodule	1	(0.6)
Pain	1	(0.6)
Pitting Oedema	1	(0.6)
Pyrexia	8	(4.5)
Thirst	1	(0.6)
Hepatobiliary Disorders	3	(1.7)
Cholecystitis Acute	1	(0.6)
Cholestasis	1	(0.6)
Cytolytic Hepatitis	1	(0.6)
Hepatomegaly	1	(0.6)
Hepatosplenomegaly	1	(0.6)
Hyperbilirubinaemia	1	(0.6)
Liver Tenderness	1	(0.6)
Portal Hypertension	1	(0.6)
Immune System Disorders	4	(2.3)
Drug Hypersensitivity	1	(0.6)
Hypersensitivity	2	(1.1)

Number (%) of Patients With Specific Clinical Adverse Experiences (Incidence >0% in One or More Treatment Groups) by System Organ Class – Open-Label Post Virologic Failure (Protocols 005, 018, and 019) - *Original Application*

	MK-0518 (N = 177)	
	n	(%)
Immune System Disorders	4	(2.3)
Immune Reconstitution Syndrome	1	(0.6)
Infections And Infestations	59	(33.3)
Acarodermatitis	1	(0.6)
Anogenital Warts	2	(1.1)
Arthritis Bacterial	1	(0.6)
Bronchitis	5	(2.8)
Cellulitis	2	(1.1)
Conjunctivitis Viral	1	(0.6)
Cytomegalovirus Chorioretinitis	2	(1.1)
Folliculitis	3	(1.7)
Fungal Infection	1	(0.6)
Fungal Skin Infection	1	(0.6)
Furuncle	1	(0.6)
Gastroenteritis	2	(1.1)
Gastroenteritis Salmonella	1	(0.6)
Genital Candidiasis	1	(0.6)
Herpes Simplex	3	(1.7)
Herpes Zoster	4	(2.3)
Influenza	5	(2.8)
Localised Infection	2	(1.1)
Measles	1	(0.6)
Molluscum Contagiosum	1	(0.6)

Number (%) of Patients With Specific Clinical Adverse Experiences (Incidence >0% in One or More Treatment Groups) by System Organ Class – Open-Label Post Virologic Failure (Protocols 005, 018, and 019) - *Original Application*

	MK-0518 (N = 177)	
	n	(%)
Infections And Infestations	59	(33.3)
Nasopharyngitis	6	(3.4)
Oesophageal Candidiasis	4	(2.3)
Onychomycosis	1	(0.6)
Oral Candidiasis	4	(2.3)
Oral Hairy Leukoplakia	1	(0.6)
Otitis Externa	1	(0.6)
Paronychia	1	(0.6)
Pharyngitis	1	(0.6)
Pharyngitis Streptococcal	1	(0.6)
Pneumonia	3	(1.7)
Pneumonia Klebsiella	1	(0.6)
Progressive Multifocal Leukoencephalopathy	1	(0.6)
Respiratory Tract Infection	2	(1.1)
Rhinitis	1	(0.6)
Sepsis	1	(0.6)
Sinusitis	2	(1.1)
Staphylococcal Infection	1	(0.6)
Subcutaneous Abscess	1	(0.6)
Tinea Cruris	1	(0.6)
Tooth Abscess	1	(0.6)
Tuberculous Pleurisy	1	(0.6)
Upper Respiratory Tract Infection	5	(2.8)

Number (%) of Patients With Specific Clinical Adverse Experiences (Incidence >0% in One or More Treatment Groups) by System Organ Class – Open-Label Post Virologic Failure (Protocols 005, 018, and 019) - *Original Application*

	MK-0518 (N = 177)	
	n	(%)
Infections And Infestations	59	(33.3)
Urinary Tract Infection	2	(1.1)
Vaginal Candidiasis	1	(0.6)
Varicella	1	(0.6)
Viral Infection	1	(0.6)
Viral Sinusitis	1	(0.6)
Wound Infection	1	(0.6)
Injury, Poisoning And Procedural Complications	11	(6.2)
Accidental Overdose	1	(0.6)
Animal Bite	1	(0.6)
Ear Canal Abrasion	1	(0.6)
Eye Penetration	1	(0.6)
Hand Fracture	2	(1.1)
Human Bite	1	(0.6)
Limb Injury	1	(0.6)
Skin Injury	1	(0.6)
Skin Laceration	1	(0.6)
Thermal Burn	1	(0.6)
Wrist Fracture	1	(0.6)
Investigations	4	(2.3)
Breath Sounds Abnormal	1	(0.6)
Lymph Node Palpable	1	(0.6)
Waist Circumference Increased	1	(0.6)

Number (%) of Patients With Specific Clinical Adverse Experiences (Incidence >0% in One or More Treatment Groups) by System Organ Class – Open-Label Post Virologic Failure (Protocols 005, 018, and 019) - *Original Application*

	MK-0518 (N = 177)	
	n	(%)
Investigations	4	(2.3)
Weight Decreased	1	(0.6)
Metabolism And Nutrition Disorders	8	(4.5)
Anorexia	2	(1.1)
Diabetes Mellitus	2	(1.1)
Failure To Thrive	1	(0.6)
Gout	2	(1.1)
Hypophosphataemia	1	(0.6)
Polydipsia	1	(0.6)
Musculoskeletal And Connective Tissue Disorders	20	(11.3)
Arthralgia	1	(0.6)
Back Pain	4	(2.3)
Costochondritis	1	(0.6)
Muscle Spasms	5	(2.8)
Myalgia	3	(1.7)
Neck Pain	1	(0.6)
Osteonecrosis	1	(0.6)
Pain In Extremity	2	(1.1)
Synovial Cyst	1	(0.6)
Tendon Disorder	1	(0.6)
Tendonitis	3	(1.7)
Neoplasms Benign, Malignant And Unspecified (Incl Cysts And Polyps)	2	(1.1)
Basal Cell Carcinoma	1	(0.6)

Number (%) of Patients With Specific Clinical Adverse Experiences (Incidence >0% in One or More Treatment Groups) by System Organ Class – Open-Label Post Virologic Failure (Protocols 005, 018, and 019) - *Original Application*

	MK-0518 (N = 177)	
	n	(%)
Neoplasms Benign, Malignant And Unspecified (Incl Cysts And Polyps)	2	(1.1)
Hodgkin's Disease	2	(1.1)
Nervous System Disorders	17	(9.6)
Disturbance In Attention	1	(0.6)
Dizziness	2	(1.1)
Dysgeusia	1	(0.6)
Facial Neuralgia	1	(0.6)
Headache	8	(4.5)
Hypoaesthesia	1	(0.6)
Hypogeusia	1	(0.6)
Hyposmia	1	(0.6)
Memory Impairment	1	(0.6)
Neuropathy	1	(0.6)
Neuropathy Peripheral	1	(0.6)
Sciatica	1	(0.6)
Somnolence	3	(1.7)
Psychiatric Disorders	14	(7.9)
Anxiety	1	(0.6)
Depression	4	(2.3)
Euphoric Mood	1	(0.6)
Hallucination	1	(0.6)
Insomnia	4	(2.3)
Libido Decreased	1	(0.6)

Number (%) of Patients With Specific Clinical Adverse Experiences (Incidence >0% in One or More Treatment Groups) by System Organ Class – Open-Label Post Virologic Failure (Protocols 005, 018, and 019) - *Original Application*

	MK-0518 (N = 177)	
	n	(%)
Psychiatric Disorders	14	(7.9)
Panic Attack	1	(0.6)
Post-Traumatic Stress Disorder	1	(0.6)
Sleep Disorder	1	(0.6)
Sopor	1	(0.6)
Suicidal Ideation	1	(0.6)
Renal And Urinary Disorders	3	(1.7)
Nephrolithiasis	1	(0.6)
Polyuria	1	(0.6)
Renal Colic	1	(0.6)
Reproductive System And Breast Disorders	5	(2.8)
Benign Prostatic Hyperplasia	1	(0.6)
Erectile Dysfunction	2	(1.1)
Genital Lesion	1	(0.6)
Pelvic Pain	1	(0.6)
Respiratory, Thoracic And Mediastinal Disorders	12	(6.8)
Allergic Respiratory Symptom	1	(0.6)
Cough	6	(3.4)
Dyspnoea	1	(0.6)
Dyspnoea Exertional	1	(0.6)
Hyperventilation	1	(0.6)
Nasal Congestion	1	(0.6)
Productive Cough	1	(0.6)

Number (%) of Patients With Specific Clinical Adverse Experiences (Incidence >0% in One or More Treatment Groups) by System Organ Class – Open-Label Post Virologic Failure (Protocols 005, 018, and 019) - *Original Application*

	MK-0518 (N = 177)	
	n	(%)
Respiratory, Thoracic And Mediastinal Disorders	12	(6.8)
Pulmonary Congestion	1	(0.6)
Rhinitis Allergic	1	(0.6)
Rhinitis Seasonal	1	(0.6)
Skin And Subcutaneous Tissue Disorders	22	(12.4)
Dermatitis Contact	1	(0.6)
Dyshidrosis	1	(0.6)
Eczema	2	(1.1)
Erythema	1	(0.6)
Henoch-Schonlein Purpura	1	(0.6)
Hyperkeratosis	1	(0.6)
Lipodystrophy Acquired	1	(0.6)
Night Sweats	1	(0.6)
Pruritus	3	(1.7)
Rash	5	(2.8)
Rash Macular	1	(0.6)
Rash Maculo-Papular	1	(0.6)
Rash Pruritic	1	(0.6)
Skin Fissures	1	(0.6)
Skin Lesion	2	(1.1)
Skin Ulcer	1	(0.6)
Subcutaneous Nodule	2	(1.1)
Vascular Disorders	2	(1.1)

Number (%) of Patients With Specific Clinical Adverse Experiences (Incidence >0% in One or More Treatment Groups) by System Organ Class – Open-Label Post Virologic Failure (Protocols 005, 018, and 019) - *Original Application*

	MK-0518 (N = 177)	
	n	(%)
Vascular Disorders	2	(1.1)
Haematoma	1	(0.6)
Varicose Vein	1	(0.6)

Although a patient may have had two or more clinical adverse experiences, the patient is counted only once within a category. The same patient may appear in different categories.

Note: MK-0518 and Placebo were administered with Optimized Background Therapy (OBT).

Adverse experience terms are from MedDRA Version 9.1.

[Ref. 5.3.5.1: P005, P018, P019]

Appendix 2.7.4: 31

Number (%) of Patients With Specific Drug-Related (Overall) Clinical Adverse Experiences (Incidence >0% in One or More Treatment Groups) by System Organ Class——Open-Label Post Virologic Failure (Protocols 005, 018, and 019) - *Cumulative Data*

	MK-0518 (N = 223)	
	n	(%)
Patients With One Or More Adverse Experiences	54	(24.2)
Patients With No Adverse Experience	169	(75.8)
Blood And Lymphatic System Disorders	1	(0.4)
Anaemia	1	(0.4)
Gastrointestinal Disorders	14	(6.3)
Abdominal Pain	3	(1.3)
Constipation	1	(0.4)
Diarrhoea	7	(3.1)
Dry Mouth	1	(0.4)
Duodenitis	1	(0.4)
Dyspepsia	1	(0.4)
Flatulence	1	(0.4)
Nausea	3	(1.3)
Salivary Hypersecretion	1	(0.4)
General Disorders And Administration Site Conditions	13	(5.8)
Asthenia	1	(0.4)
Chills	1	(0.4)
Drug Intolerance	1	(0.4)
Fatigue	2	(0.9)
Feeling Hot	1	(0.4)
Injection Site Erythema	1	(0.4)

Number (%) of Patients With Specific Drug-Related (Overall) Clinical Adverse Experiences (Incidence >0% in One or More Treatment Groups) by System Organ Class——Open-Label Post Virologic Failure (Protocols 005, 018, and 019) - *Cumulative Data*

	MK-0518 (N = 223)	
	n	(%)
General Disorders And Administration Site Conditions	13	(5.8)
Injection Site Nodule	1	(0.4)
Injection Site Reaction	4	(1.8)
Nodule	1	(0.4)
Pain	1	(0.4)
Pyrexia	3	(1.3)
Thirst	1	(0.4)
Hepatobiliary Disorders	1	(0.4)
Cholestasis	1	(0.4)
Cytolytic Hepatitis	1	(0.4)
Hepatosplenomegaly	1	(0.4)
Hyperbilirubinaemia	1	(0.4)
Immune System Disorders	1	(0.4)
Immune Reconstitution Syndrome	1	(0.4)
Infections And Infestations	1	(0.4)
Herpes Zoster	1	(0.4)
Investigations	1	(0.4)
Blood Creatine Increased	1	(0.4)
Metabolism And Nutrition Disorders	6	(2.7)
Diabetes Mellitus	1	(0.4)
Facial Wasting	1	(0.4)
Gout	1	(0.4)

Number (%) of Patients With Specific Drug-Related (Overall) Clinical Adverse Experiences (Incidence >0% in One or More Treatment Groups) by System Organ Class——Open-Label Post Virologic Failure (Protocols 005, 018, and 019) - *Cumulative Data*

	MK-0518 (N = 223)	
	n	(%)
Metabolism And Nutrition Disorders	6	(2.7)
Hyperlipidaemia	2	(0.9)
Hypophosphataemia	1	(0.4)
Polydipsia	1	(0.4)
Musculoskeletal And Connective Tissue Disorders	7	(3.1)
Muscle Spasms	4	(1.8)
Myalgia	3	(1.3)
Nodule On Extremity	1	(0.4)
Nervous System Disorders	9	(4.0)
Balance Disorder	1	(0.4)
Dysgeusia	1	(0.4)
Headache	3	(1.3)
Hypogeusia	1	(0.4)
Hyposmia	1	(0.4)
Neuropathy Peripheral	1	(0.4)
Somnolence	2	(0.9)
Psychiatric Disorders	4	(1.8)
Depression	1	(0.4)
Euphoric Mood	1	(0.4)
Insomnia	1	(0.4)
Sleep Disorder	1	(0.4)
Renal And Urinary Disorders	1	(0.4)

Number (%) of Patients With Specific Drug-Related (Overall) Clinical Adverse Experiences (Incidence >0% in One or More Treatment Groups) by System Organ Class——Open-Label Post Virologic Failure (Protocols 005, 018, and 019) - *Cumulative Data*

	MK-0518 (N = 223)	
	n	(%)
Renal And Urinary Disorders	1	(0.4)
Polyuria	1	(0.4)
Skin And Subcutaneous Tissue Disorders	14	(6.3)
Lipodystrophy Acquired	1	(0.4)
Night Sweats	1	(0.4)
Rash	5	(2.2)
Rash Papular	1	(0.4)
Skin Discolouration	1	(0.4)
Skin Ulcer	1	(0.4)
Subcutaneous Nodule	4	(1.8)
Vascular Disorders	2	(0.9)
Hypertension	1	(0.4)
Thrombophlebitis	1	(0.4)

Although a patient may have had two or more drug-related clinical adverse experiences, the patient is counted only once within a category. The same patient may appear in different categories.

Note: MK-0518 and Placebo were administered with Optimized Background Therapy (OBT).

Adverse experience terms are from MedDRA Version 9.1.

[Ref. 5.3.5.1: P005-Define, P018-Define, P019-Define]

Appendix 2.7.4: 32

Number (%) of Patients With Specific Drug-Related (Overall) Clinical Adverse Experiences (Incidence >0% in One or More Treatment Groups) by System Organ Class——Open-Label Post Virologic Failure (Protocols 005, 018, and 019) - *Original Application*

	MK-0518 (N = 177)	
	n	(%)
Patients With One Or More Drug-Related Adverse Experiences	34	(19.2)
Patients With No Drug-Related Adverse Experience	143	(80.8)
Blood And Lymphatic System Disorders	1	(0.6)
Anaemia	1	(0.6)
Gastrointestinal Disorders	9	(5.1)
Abdominal Pain	2	(1.1)
Constipation	1	(0.6)
Diarrhoea	3	(1.7)
Dry Mouth	1	(0.6)
Duodenitis	1	(0.6)
Dyspepsia	1	(0.6)
Flatulence	1	(0.6)
Nausea	3	(1.7)
Salivary Hypersecretion	1	(0.6)
General Disorders And Administration Site Conditions	10	(5.6)
Chills	1	(0.6)
Drug Intolerance	1	(0.6)
Fatigue	2	(1.1)
Feeling Hot	1	(0.6)
Injection Site Reaction	3	(1.7)
Nodule	1	(0.6)
Pain	1	(0.6)

Number (%) of Patients With Specific Drug-Related (Overall) Clinical Adverse Experiences (Incidence >0% in One or More Treatment Groups) by System Organ Class—Open-Label Post Virologic Failure (Protocols 005, 018, and 019) - *Original Application*

	MK-0518 (N = 177)	
	n	(%)
General Disorders And Administration Site Conditions	10	(5.6)
Pyrexia	2	(1.1)
Thirst	1	(0.6)
Hepatobiliary Disorders	1	(0.6)
Cholestasis	1	(0.6)
Cytolytic Hepatitis	1	(0.6)
Hepatosplenomegaly	1	(0.6)
Hyperbilirubinaemia	1	(0.6)
Immune System Disorders	1	(0.6)
Immune Reconstitution Syndrome	1	(0.6)
Infections And Infestations	1	(0.6)
Herpes Zoster	1	(0.6)
Metabolism And Nutrition Disorders	3	(1.7)
Diabetes Mellitus	1	(0.6)
Gout	1	(0.6)
Hypophosphataemia	1	(0.6)
Polydipsia	1	(0.6)
Musculoskeletal And Connective Tissue Disorders	5	(2.8)
Muscle Spasms	3	(1.7)
Myalgia	2	(1.1)
Pain In Extremity	1	(0.6)
Nervous System Disorders	8	(4.5)
Dysgeusia	1	(0.6)

Number (%) of Patients With Specific Drug-Related (Overall) Clinical Adverse Experiences (Incidence >0% in One or More Treatment Groups) by System Organ Class—Open-Label Post Virologic Failure (Protocols 005, 018, and 019) - *Original Application*

	MK-0518 (N = 177)	
	n	(%)
Nervous System Disorders	8	(4.5)
Headache	3	(1.7)
Hypogeusia	1	(0.6)
Hyposmia	1	(0.6)
Neuropathy	1	(0.6)
Neuropathy Peripheral	1	(0.6)
Somnolence	2	(1.1)
Psychiatric Disorders	3	(1.7)
Euphoric Mood	1	(0.6)
Insomnia	1	(0.6)
Sleep Disorder	1	(0.6)
Renal And Urinary Disorders	1	(0.6)
Polyuria	1	(0.6)
Skin And Subcutaneous Tissue Disorders	8	(4.5)
Lipodystrophy Acquired	1	(0.6)
Night Sweats	1	(0.6)
Rash	2	(1.1)
Rash Macular	1	(0.6)
Skin Ulcer	1	(0.6)
Subcutaneous Nodule	2	(1.1)

Although a patient may have had two or more drug-related clinical adverse experiences, the patient is counted only once within a category. The same patient may appear in different categories.

Note: MK-0518 and Placebo were administered with Optimized Background Therapy (OBT).

Adverse experience terms are from MedDRA Version 9.1.

[Ref. 5.3.5.1: P005, P018, P019]

Appendix 2.7.4: 33

Laboratory Adverse Experience Summary—Open-Label Post Virologic Failure
(Protocols 005, 018, and 019) - *Cumulative Data*

	MK-0518 (N = 223)	
	n	(%)†
Number (%) of patients:		
With at least one lab test postbaseline	223	
With one or more adverse experiences	45	(20.2)
With no adverse experience	178	(79.8)
With drug-related‡ adverse experiences	22	(9.9)
With serious adverse experiences	0	(0.0)
With serious drug-related adverse experiences	0	(0.0)
Who died	0	(0.0)
Discontinued due to adverse experiences	0	(0.0)
Discontinued due to drug-related adverse experiences	0	(0.0)
Discontinued due to serious adverse experiences	0	(0.0)
Discontinued due to serious drug-related adverse experiences	0	(0.0)

† The percent = Number of patients within the laboratory adverse experience category / number of patients with one or more laboratory tests postbaseline

‡ Determined by the investigator to be possibly, probably or definitely drug-related.

Although a patient may have had two or more drug-related clinical adverse experiences, the patient is counted only once within a category. The same patient may appear in different categories.

Note: MK-0518 and Placebo were administered with Optimized Background Therapy (OBT).

[Ref. 5.3.5.1: P005-Define, P018-Define, P019-Define]

Appendix 2.7.4: 34

Laboratory Adverse Experience Summary—Open-Label Post Virologic Failure
(Protocols 005, 018, and 019) - *Original Application*

	MK-0518 (N = 177)	
	n	(%)[†]
Number (%) of patients:		
With at least one lab test postbaseline	177	
With one or more adverse experiences	23	(13.0)
With no adverse experience	154	(87.0)
With drug-related[‡] adverse experiences	11	(6.2)
With serious adverse experiences	0	(0.0)
With serious drug-related adverse experiences	0	(0.0)
Who died	0	(0.0)
Discontinued due to adverse experiences	0	(0.0)
Discontinued due to drug-related adverse experiences	0	(0.0)
Discontinued due to serious adverse experiences	0	(0.0)
Discontinued due to serious drug-related adverse experiences	0	(0.0)

[†] The percent = Number of patients within the laboratory adverse experience category / number of patients with one or more laboratory tests postbaseline

[‡] Determined by the investigator to be possibly, probably or definitely drug-related.

Although a patient may have had two or more drug-related clinical adverse experiences, the patient is counted only once within a category. The same patient may appear in different categories.

Note: MK-0518 and Placebo were administered with Optimized Background Therapy (OBT).

[Ref. 5.3.5.1: P005, P018, P019]

Appendix 2.7.4: 35

Number (%) of Patients With Specific Laboratory Adverse Experiences (Incidence >0% in One or More Treatment Groups) by Laboratory Test Category – Open-Label Post Virologic Failure (Protocols 005, 018, and 019) - *Cumulative Data*

	MK-0518 (N=223)	
	n/m	(%)
Patients with one or more adverse experiences	45/223	(20.2)
Patients with no adverse experiences	178/223	(79.8)
Blood Chemistry Test	**36/223**	**(16.1)**
Alanine aminotransferase increased	6/223	(2.7)
Aspartate aminotransferase increased	5/223	(2.2)
Blood amylase increased	1/223	(0.4)
Blood bilirubin increased	4/223	(1.8)
Blood cholesterol increased	4/222	(1.8)
Blood creatinine increased	4/223	(1.8)
Blood glucose increased	3/223	(1.3)
Blood pancreatic amylase increased	2/28	(7.1)
Blood phosphorus decreased	7/223	(3.1)
Blood phosphorus increased	1/223	(0.4)
Blood potassium decreased	1/223	(0.4)
Blood triglycerides increased	5/222	(2.3)
Creatine phosphokinase increased	5/223	(2.2)
Lipase increased	1/223	(0.4)
Low density lipoprotein increased	1/209	(0.5)
Protein total decreased	1/223	(0.4)
Clinical Microbiology Test	**1/18**	**(5.6)**

Number (%) of Patients With Specific Laboratory Adverse Experiences (Incidence >0% in One or More Treatment Groups) by Laboratory Test Category – Open-Label Post Virologic Failure (Protocols 005, 018, and 019) - *Cumulative Data*

	MK-0518 (N=223)	
	n/m	(%)
Clinical Microbiology Test	**1/18**	**(5.6)**
Virus culture positive	1/1	(100.0)
Hematology Laboratory Test	**9/223**	**(4.0)**
Absolute lymphocyte count decreased	1/223	(0.4)
Absolute neutrophil count decreased	3/223	(1.3)
Haemoglobin decreased	2/223	(0.9)
Platelet count decreased	1/223	(0.4)
Red blood cell count decreased	1/223	(0.4)
White blood cell count decreased	1/223	(0.4)
Urinalysis Test	**3/221**	**(1.4)**
Blood urine present	1/221	(0.5)
Protein urine present	1/221	(0.5)
Red blood cells urine positive	1/221	(0.5)
The Following Laboratory Adverse Experiences Could Not Be Categorized	**1/†**	

Number (%) of Patients With Specific Laboratory Adverse Experiences (Incidence >0% in One or More Treatment Groups) by Laboratory Test Category – Open-Label Post Virologic Failure (Protocols 005, 018, and 019) - *Cumulative Data*

	MK-0518 (N=223)	
	n/m	(%)
The Following Laboratory Adverse Experiences Could Not Be Categorized	**1/†**	
Cytomegalovirus antigen positive	1/†	

† indicates that there was no associated laboratory test or there were no patients for whom the laboratory test was recorded postbaseline.

Although a patient may have had two or more laboratory adverse experiences, the patient is counted only once in a category. The same patient may appear in different categories.

Note: MK-0518 and Placebo were administered with Optimized Background Therapy (OBT).

Adverse experience terms are from MedDRA Version 9.1.

n/m = Number of patients with laboratory adverse experiences / number of patients for whom the laboratory test was recorded postbaseline.

[Ref. 5.3.5.1: P005-Define, P018-Define, P019-Define]

Appendix 2.7.4: 36

Number (%) of Patients With Specific Laboratory Adverse Experiences (Incidence >0% in One or More Treatment Groups) by Laboratory Test Category – Open-Label Post Virologic Failure (Protocols 005, 018, and 019) - *Original Application*

	MK-0518 (N=177)	
	n/m	(%)
Patients with one or more adverse experiences	23/177	(13.0)
Patients with no adverse experiences	154/177	(87.0)
Blood Chemistry Test	**15/177**	**(8.5)**
Alanine aminotransferase increased	1/177	(0.6)
Aspartate aminotransferase increased	1/177	(0.6)
Blood amylase increased	1/177	(0.6)
Blood bilirubin increased	4/177	(2.3)
Blood creatinine increased	2/177	(1.1)
Blood glucose increased	2/177	(1.1)
Blood pancreatic amylase increased	1/23	(4.3)
Blood phosphorus decreased	5/177	(2.8)
Blood triglycerides increased	1/176	(0.6)
Creatine phosphokinase increased	3/177	(1.7)
Clinical Microbiology Test	**1/12**	**(8.3)**
Virus culture positive	1/1	(100.0)
Hematology Laboratory Test	**6/177**	**(3.4)**
Absolute lymphocyte count decreased	1/177	(0.6)

Number (%) of Patients With Specific Laboratory Adverse Experiences (Incidence >0% in One or More Treatment Groups) by Laboratory Test Category – Open-Label Post Virologic Failure (Protocols 005, 018, and 019) - *Original Application*

	MK-0518 (N=177)	
	n/m	(%)
Hematology Laboratory Test	**6/177**	**(3.4)**
Absolute neutrophil count decreased	3/177	(1.7)
Red blood cell count decreased	1/177	(0.6)
White blood cell count decreased	1/177	(0.6)
Urinalysis Test	**3/175**	**(1.7)**
Blood urine present	1/175	(0.6)
Protein urine present	1/175	(0.6)
Red blood cells urine positive	1/175	(0.6)
The Following Laboratory Adverse Experiences Could Not Be Categorized	**1/†**	
Cytomegalovirus antigen positive	1/†	

† indicates that there was no associated laboratory test or there were no patients for whom the laboratory test was recorded postbaseline.

Although a patient may have had two or more laboratory adverse experiences, the patient is counted only once in a category. The same patient may appear in different categories.

Note: MK-0518 and Placebo were administered with Optimized Background Therapy (OBT).

Adverse experience terms are from MedDRA Version 9.1.

n/m = Number of patients with laboratory adverse experiences / number of patients for whom the laboratory test was recorded postbaseline.

[Ref. 5.3.5.1: P005, P018, P019]

Appendix 2.7.4: 37

Number (%) of Patients With Specific Drug-Related (Overall) Laboratory Adverse Experiences (Incidence >0% in One or More Treatment Groups) by Laboratory Test Category – Open-Label Post Virologic Failure (Protocols 005, 018, and 019) - *Cumulative Data*

	MK-0518 (N=223)	
	n/m	(%)
Patients with one or more adverse experiences	22/223	(9.9)
Patients with no adverse experiences	201/223	(90.1)
Blood Chemistry Test	**20/223**	**(9.0)**
Alanine aminotransferase increased	2/223	(0.9)
Aspartate aminotransferase increased	2/223	(0.9)
Blood bilirubin increased	3/223	(1.3)
Blood cholesterol increased	4/222	(1.8)
Blood creatinine increased	1/223	(0.4)
Blood glucose increased	2/223	(0.9)
Blood pancreatic amylase increased	1/28	(3.6)
Blood phosphorus decreased	6/223	(2.7)
Blood triglycerides increased	2/222	(0.9)
Creatine phosphokinase increased	1/223	(0.4)
Lipase increased	1/223	(0.4)
Low density lipoprotein increased	1/209	(0.5)

Number (%) of Patients With Specific Drug-Related (Overall) Laboratory Adverse Experiences (Incidence >0% in One or More Treatment Groups) by Laboratory Test Category – Open-Label Post Virologic Failure (Protocols 005, 018, and 019) - *Cumulative Data*

	MK-0518 (N=223)	
	n/m	(%)
Hematology Laboratory Test	**3/223**	**(1.3)**
Absolute neutrophil count decreased	2/223	(0.9)
Haemoglobin decreased	1/223	(0.4)

Although a patient may have had two or more drug-related laboratory adverse experiences, the patient is counted only once in a category. The same patient may appear in different categories.

Note: MK-0518 and Placebo were administered with Optimized Background Therapy (OBT).

Adverse experience terms are from MedDRA Version 9.1

n/m = Number of patients with laboratory adverse experiences / number of patients for whom the laboratory test was recorded postbaseline.

[Ref. 5.3.5.1: P005-Define, P018-Define, P019-Define]

Appendix 2.7.4: 38

Number (%) of Patients With Specific Drug-Related (Overall) Laboratory Adverse Experiences (Incidence >0% in One or More Treatment Groups) by Laboratory Test Category – Open-Label Post Virologic Failure (Protocols 005, 018, and 019) - *Original Application*

	MK-0518 (N=177)	
	n/m	(%)
Patients with one or more drug-related adverse experiences	11/177	(6.2)
Patients with no drug-related adverse experiences	166/177	(93.8)
Blood Chemistry Test	**9/177**	**(5.1)**
Blood bilirubin increased	2/177	(1.1)
Blood creatinine increased	1/177	(0.6)
Blood glucose increased	1/177	(0.6)
Blood phosphorus decreased	5/177	(2.8)
Creatine phosphokinase increased	1/177	(0.6)
Hematology Laboratory Test	**3/177**	**(1.7)**
Absolute lymphocyte count decreased	1/177	(0.6)
Absolute neutrophil count decreased	2/177	(1.1)

Although a patient may have had two or more drug-related laboratory adverse experiences, the patient is counted only once in a category. The same patient may appear in different categories.

Note: MK-0518 and Placebo were administered with Optimized Background Therapy (OBT).

Adverse experience terms are from MedDRA Version 9.1

n/m = Number of patients with laboratory adverse experiences / number of patients for whom the laboratory test was recorded postbaseline.

[Ref. 5.3.5.1: P005, P018, P019]

Appendix 2.7.4: 39

Narratives for Patients with Adverse Experiences Resulting in Death During the SUR Period (as Reported in Either the WAES or CTS Databases as of [redacted])

Protocol 005 - MK-0518 200 mg b.i.d. group

AN 3261, a 36-year old white male with lipodystrophy, anorexia, and a history of tuberculosis, diarrhea, hematuria, and urethritis was randomized on Day 1 ([redacted]) to receive MK-0518 200 mg b.i.d. in combination with OBT of lamivudine plus zidovudine and lopinavir plus ritonavir, and tenofovir disoproxil fumarate. On Day 337 ([redacted]) the patient entered the open-label phase of the study and was placed on MK-0518 400 mg b.i.d. in combination with ongoing OBT. On Day 155 ([redacted]), the patient underwent an abdominal ultrasound due to complaints of abdominal pain, weight loss, and sudoresis (diaphoresis) at night. The ultrasound revealed two splenic abscesses and adenomegaly. On Day 158 ([redacted]), the patient was hospitalized to investigate disseminated tuberculosis. Abdominal CT performed which revealed splenic abscess, adenomegaly and ascites. Empiric therapy for tuberculosis was started. On Day 170 ([redacted]), the patient improved and was discharged with persisting splenic abscess and adenomegaly. Patient hospitalized again on Day 175 ([redacted]) due to dyspnea and intense sweats. Chest X ray and gasometry revealed pleural effusion. On Day 179 ([redacted]), the patient interrupted all study therapy including OBT. Subsequently, the patient developed hyperkalemia, hyperphosphatemia, LDH increased, and renal impairment and died on Day 194 ([redacted]). Final diagnosis has not been determined and is pending histopathology report. The investigator determined that splenic abscess, adenomegaly, and pleural effusion were definitely not related to study drug therapy including OBT.

Protocol 005 - Open-Label Extension (MK-0518)

AN 3264, a 43-year-old Hispanic male with CD4 lymphocytes decreased, dyslipidemia, paresthesia foot, AIDS, lipodystrophy and a history of cryptococcosis, mycobacterium tuberculosis, and HIV wasting syndrome was randomized on Day 1 ([redacted]) to receive placebo in combination with OBT of didanosine, abacavir sulfate, lopinavir (+) ritonavir, and saquinavir. Patient switched to open-label MK-0518, 600 mg b.i.d. on Day 170 ([redacted]) and then was changed to open-label MK-0518 400 mg b.i.d. on Day 367 ([redacted]). The site was informed that the patient experienced gastroenteritis and was hospitalized on [redacted]. On [redacted] the patient died. The cause of death was gastroenteritis. The reporting investigator felt that gastroenteritis was not related to study therapy.

Protocol 019 - MK-0518 400 mg b.i.d. group

AN 7005, a 60-year old white male with a history of chronic prostatitis, HIV encephalitis, Kaposi's sarcoma, pneumoocystis carinii pneumonia, and septic shock was randomized on Day 1 ([redacted]) to receive MK-0518 400 mg b.i.d. in combination with OBT of ritonavir, darunavir, enfuvirtide, and abacavir sulfate (+) lamivudine. On Day 76 ([redacted]), clinical examination revealed adenopathy and buccal ulcerations. On Day 84 ([redacted]), the patient was started on therapy with thalidomide for buccal ulcerations. On Day 86 ([redacted]), there was an improvement of lesions but axillary and maxillary lymph nodes were noted with suspected diagnosis of lymphoma. On Day 88 ([redacted]), the patient was hospitalized for lymph node biopsy which showed large B-cell lymphoma. Study therapy continued. On Day 99 ([redacted]), the patient was hospitalized for fever and general health status deterioration and received the first course of chemotherapy on Day 111 ([redacted]). During this hospitalization, the patient experienced septic shock due to bacterial prostate infection. On Day 120 ([redacted]), an MRI of the brain was performed which confirmed HIV encephalitis. The patient received four more courses of chemotherapy (last course was on Day 222 [redacted]). On Day 233 ([redacted]), the patient was hospitalized for polyuria and cough and also experienced diarrhea. Final diagnosis was diarrhea and prostatitis due to E. coli. The patient subsequently recovered and was discharged. On Day 251 ([redacted]), the patient entered the open-label phase and was placed on therapy with MK-0518, 400 mg b.i.d. in combination with OBT of abacavir (+) lamivudine (+) zidovudine. On Day 2 of the open-label phase ([redacted]), the patient was hospitalized with the diagnosis of CMV infection and placed on therapy with foscavir (IV). Patient was discharged on Day 17 of open-label phase ([redacted]). On Day 29 of the open-label phase ([redacted]), the patient was hospitalized for implantable chamber septicemia and was withdrawn from the study. The patient subsequently died due to end stage AIDS on [redacted] The reporting investigator felt that B-cell lymphoma was probably not related to study therapy and septic shock was definitely not related to study therapy.

AN 16318, a 50-year old white male with a history of hypertension, panic disorder, neurodermatitis, lymphoedema, azithromycin, doxycycline, cefadroxil and penicillin allergy, folliculitis, Kaposi's sarcoma, pneumoocystis carinii pneumonia, and chronic pulmonary heart disease was randomized on Day 1 ([redacted]) to receive MK-0518 400 mg b.i.d. in combination with OBT of darunavir, emtricitabine (+) tenofovir disoproxil fumarate, and ritonavir. On Day 70 ([redacted]), the patient was hospitalized due to moderate cellulitis of the left leg and was placed on vancomycin therapy. Study therapy continued. Blood cultures were negative and on Day 84 ([redacted]), cellulitis resolved. The reporting investigator considered the cellulitis probably not related to study therapy. On Day 197 ([redacted]), the patient was hospitalized with cough, dyspnea, and malaise. A chest x-ray revealed suspected pulmonary edema.

The patient was started on ceftriaxone sodium. ECG was notable for nonspecific ST depression. Therapeutic heparin and nitroglycerin drip were started. Study therapy continued. Coronary angiography was performed which revealed severe three vessel coronary artery disease. A CABG was recommended. Subsequently patient's condition worsened with speculation as to the development of acute LAD occlusion which was not confirmed. The patient subsequently died on Day 200 ([redacted]). The reporting investigator considered coronary artery disease as probably not related to study therapy.

Appendix 2.7.4: 40

Number (%) of Patients With Specific Serious Clinical Adverse Experiences (Incidence >0% in One or More Treatment Groups) by System Organ Class (Protocol 004: Cohorts I and II Combined; Combination Therapy Phase, Entire Study Period) - *Cumulative Data*

	MK-0518 100 mg b.i.d. (N = 39)		MK-0518 200 mg b.i.d. (N = 40)		MK-0518 400 mg b.i.d. (N = 41)		MK-0518 600 mg b.i.d. (N = 40)		Efavirenz 600 mg q.d. (N = 38)		Total (N = 198)	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Patients With One Or More Adverse Experiences	2	(5.1)	5	(12.5)	2	(4.9)	2	(5.0)	3	(7.9)	14	(7.1)
Patients With No Adverse Experience	37	(94.9)	35	(87.5)	39	(95.1)	38	(95.0)	35	(92.1)	184	(92.9)
Eye Disorders	0	(0.0)	1	(2.5)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.5)
Retinal Vein Occlusion	0	(0.0)	1	(2.5)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.5)
Gastrointestinal Disorders	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(2.6)	1	(0.5)
Abdominal Pain	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(2.6)	1	(0.5)
General Disorders And Administration Site Conditions	0	(0.0)	0	(0.0)	0	(0.0)	1	(2.5)	0	(0.0)	1	(0.5)
Chest Pain	0	(0.0)	0	(0.0)	0	(0.0)	1	(2.5)	0	(0.0)	1	(0.5)
Infections And Infestations	1	(2.6)	3	(7.5)	0	(0.0)	0	(0.0)	1	(2.6)	5	(2.5)
Amoebic Dysentery	0	(0.0)	1	(2.5)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.5)
Cellulitis	0	(0.0)	1	(2.5)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.5)
Pharyngitis	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(2.6)	1	(0.5)
Pneumonia	0	(0.0)	1	(2.5)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.5)
Pyelonephritis	1	(2.6)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.5)
Injury, Poisoning And Procedural Complications	1	(2.6)	0	(0.0)	1	(2.4)	1	(2.5)	0	(0.0)	3	(1.5)
Device Malfunction	0	(0.0)	0	(0.0)	0	(0.0)	1	(2.5)	0	(0.0)	1	(0.5)
Intentional Overdose	1	(2.6)	0	(0.0)	1	(2.4)	0	(0.0)	0	(0.0)	2	(1.0)
Neoplasms Benign, Malignant And Unspecified (Incl Cysts And Polyps)	0	(0.0)	0	(0.0)	1	(2.4)	0	(0.0)	1	(2.6)	2	(1.0)
Kaposi's Sarcoma	0	(0.0)	0	(0.0)	1	(2.4)	0	(0.0)	0	(0.0)	1	(0.5)

Number (%) of Patients With Specific Serious Clinical Adverse Experiences (Incidence >0% in One or More Treatment Groups) by System Organ Class (Protocol 004: Cohorts I and II Combined; Combination Therapy Phase, Entire Study Period) - *Cumulative Data*

	MK-0518 100 mg b.i.d. (N = 39)		MK-0518 200 mg b.i.d. (N = 40)		MK-0518 400 mg b.i.d. (N = 41)		MK-0518 600 mg b.i.d. (N = 40)		Efavirenz 600 mg q.d. (N = 38)		Total (N = 198)	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Neoplasms Benign, Malignant And Unspecified (Incl Cysts And Polyps)	0	(0.0)	0	(0.0)	1	(2.4)	0	(0.0)	1	(2.6)	2	(1.0)
Squamous Cell Carcinoma	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(2.6)	1	(0.5)
Nervous System Disorders	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(2.6)	1	(0.5)
Cervicobrachial Syndrome	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(2.6)	1	(0.5)
Psychiatric Disorders	1	(2.6)	0	(0.0)	1	(2.4)	0	(0.0)	0	(0.0)	2	(1.0)
Alcoholism	0	(0.0)	0	(0.0)	1	(2.4)	0	(0.0)	0	(0.0)	1	(0.5)
Depression	1	(2.6)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.5)
Suicidal Ideation	1	(2.6)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.5)
Renal And Urinary Disorders	0	(0.0)	1	(2.5)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.5)
Calculus Urinary	0	(0.0)	1	(2.5)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.5)

Although a patient may have had two or more clinical adverse experiences, the patient is counted only once within a category. The same patient may appear in different categories.

Adverse experience terms are from MedDRA Version 9.1.

[Ref. 5.3.5.1: P004-Define]

Appendix 2.7.4: 41

Listing of Patients With Serious Clinical Adverse Experiences
(Protocol 004: Cohorts I and II Combined; Combination Therapy Phase, Entire Study Period) - *Cumulative Data*

Study Number	AN	Gender	Race	Age	Period	Therapy	Total Daily Dose	Relative Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontinuance†	Intensity	Serious	Drug Relationship	Action Taken	Outcome
MK-0518 100 mg b.i.d.																
0040001	398	M	white	38 yr	Treatment II	Lamivudine	300.00 mg	60	Depression	9 day	524	severe	Y	prob not	interrupted PRx	recovered
						MK-0518	200.00 mg									
						Tenofovir	300.00 mg									
						Lamivudine	300.00 mg	64	Intentional overdose	2 day	524	mod	Y	prob not	interrupted PRx	recovered
						MK-0518	200.00 mg									
						Tenofovir	300.00 mg									
						Lamivudine	300.00 mg	64	Suicidal ideation	5 day	524	severe	Y	prob not	interrupted PRx	recovered
						MK-0518	200.00 mg									
						Tenofovir	300.00 mg									
0040018	379	F	multi	34 yr	Treatment II	Lamivudine	300.00 mg	48	Pyelonephritis	5 day	504	mod	Y	prob not	no action with test drug	recovered
						MK-0518	200.00 mg									
						Tenofovir	300.00 mg									
MK-0518 200 mg b.i.d.																

Listing of Patients With Serious Clinical Adverse Experiences
(Protocol 004: Cohorts I and II Combined; Combination Therapy Phase, Entire Study Period) - *Cumulative Data*

Study Number	AN	Gender	Race	Age	Period	Therapy	Total Daily Dose	Relative Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontinuance†	Intensity	Serious	Drug Relationship	Action Taken	Outcome
MK-0518 200 mg b.i.d.																
0040001	399	M	white	56 yr	Treatment II	Lamivudine	300.00 mg	61	Retinal vein occlusion	CONT	72	mod	Y	prob not	no action with test drug	not recovered
						MK-0518	400.00 mg									
						Tenofovir	300.00 mg									
0040020	91	M	white	26 yr	Treatment II	Lamivudine	300.00 mg	344	Cellulitis	10 day	619	severe	Y	def not	no action with test drug	recovered
						MK-0518	400.00 mg									
						Tenofovir	300.00 mg									
0040026	106	M	Hispa	23 yr	Treatment II	Lamivudine	300.00 mg	93	Amoebic dysentery	4 day	496	mod	Y	def not	no action with test drug	recovered
						MK-0518	400.00 mg									
						Tenofovir	300.00 mg									
	349	M	Hispa	30 yr	Treatment II	Lamivudine	300.00 mg	28	Calculus urinary	7 day	492	severe	Y	def not	no action with test drug	recovered
						MK-0518	400.00 mg									
						Tenofovir	300.00 mg									

Listing of Patients With Serious Clinical Adverse Experiences
(Protocol 004: Cohorts I and II Combined; Combination Therapy Phase, Entire Study Period) - *Cumulative Data*

Study Number	AN	Gender	Race	Age	Period	Therapy	Total Daily Dose	Relative Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontinuance†	Intensity	Serious	Drug Relationship	Action Taken	Outcome
MK-0518 200 mg b.i.d.																
0040026	349	M	Hispa	30 yr	Treatment II	Lamivudine	300.00 mg	80	Calculus urinary	3 day	492	severe	Y	def not	no action with test drug	recovered
						MK-0518	400.00 mg									
						Tenofovir	300.00 mg									
0040030	141	F	Asian	45 yr	Treatment II	Lamivudine	300.00 mg	335	Pneumonia	11 day	340	mod	Y	prob not	no action with test drug	recovered
						Tenofovir	300.00 mg									
MK-0518 400 mg b.i.d.																
0040003	17	M	Hispa	37 yr	Post-Treatment Ext	Off Drug 1 day		502	Intentional overdose	8 day	501	severe	Y	prob not	discontinued PRx	recovered
0040017	**12**	**M**	**white**	**55 yr**	**Treatment II**	**Lamivudine**	**300.00 mg**	**409**	**Kaposi's sarcoma**	**16 day**	**604**	**mod**	**Y**	**def not**	**no action with test drug**	**recovered**
						MK-0518	**800.00 mg**									
						Tenofovir	**300.00 mg**									

Listing of Patients With Serious Clinical Adverse Experiences
(Protocol 004: Cohorts I and II Combined; Combination Therapy Phase, Entire Study Period) - *Cumulative Data*

Study Number	AN	Gender	Race	Age	Period	Therapy	Total Daily Dose	Relative Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontinuance†	Intensity	Serious	Drug Relationship	Action Taken	Outcome
MK-0518 400 mg b.i.d.																
0040017	12	M	white	55 yr	Extension	Lamivudine	300.00 mg	540	Alcoholism	9 day	604	severe	Y	def not	no action with test drug	recovered
						MK-0518	800.00 mg									
						Tenofovir	300.00 mg									
MK-0518 600 mg b.i.d.																
0040008	90	M	white	49 yr	Treatment II	Lamivudine	300.00 mg	410	Device malfunction	4 day	654	mod	Y	def not	no action with test drug	recovered
						MK-0518	1200.00 mg									
						Tenofovir	300.00 mg									
0040020	10	M	white	39 yr	Treatment II	Lamivudine	300.00 mg	345	Chest pain	2 day	617	severe	Y	prob not	no action with test drug	recovered
						MK-0518	1200.00 mg									
						Tenofovir	300.00 mg									
Efavirenz 600 mg q.d.																

Listing of Patients With Serious Clinical Adverse Experiences
(Protocol 004: Cohorts I and II Combined; Combination Therapy Phase, Entire Study Period) - *Cumulative Data*

Study Number	AN	Gender	Race	Age	Period	Therapy	Total Daily Dose	Relative Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontinuance†	Intensity	Serious	Drug Relationship	Action Taken	Outcome
Efavirenz 600 mg q.d.																
0040024	353	M	white	38 yr	Treatment II	Efavirenz	600.00 mg	40	Abdominal pain	2.43 mo	259	severe	Y	prob not	no action with test drug	recovered
						Lamivudine	300.00 mg									
						Tenofovir	300.00 mg									
						Efavirenz	600.00 mg	139	Cervicobrachial syndrome	4 day	259	severe	Y	prob not	no action with test drug	recovered
						Lamivudine	300.00 mg									
						Tenofovir	300.00 mg									
						Efavirenz	600.00 mg	199	Cervicobrachial syndrome	10 day	259	severe	Y	prob not	no action with test drug	recovered
						Lamivudine	300.00 mg									
						Tenofovir	300.00 mg									
0040030	**153**	**F**	**Asian**	**36 yr**	**Extension**	**Efavirenz**	**600.00 mg**	**499**	**Pharyngitis**	**6 day**	**505**	**mod**	**Y**	**def not**	**no action with test drug**	**recovered**
						Lamivudine	**300.00 mg**									
						Tenofovir	**300.00 mg**									

Listing of Patients With Serious Clinical Adverse Experiences
(Protocol 004: Cohorts I and II Combined; Combination Therapy Phase, Entire Study Period) - *Cumulative Data*

Study Number	AN	Gender	Race	Age	Period	Therapy	Total Daily Dose	Relative Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontinuance[†]	Intensity	Serious	Drug Relationship	Action Taken	Outcome
Efavirenz 600 mg q.d.																
0040031	163	M	white	48 yr	Treatment II	Efavirenz Lamivudine Tenofovir	600.00 mg 300.00 mg 300.00 mg	207	Squamous cell carcinoma	6.87 mo	421	mod	Y	prob not	no action with test drug	recovered

[†]Day study therapy was discontinued relative to the start of study therapy.
Drug Relationship: def = definitely, def not = definitely not, poss = possibly, prob = probably, prob not = probably not
Intensity: mod = moderate

Note: MK-0518 and efavirenz were administered with tenofovir and lamivudine.
Adverse experience terms are from MedDRA Version 9.1.

[Ref. 5.3.5.1: P004-Define]

Appendix 2.7.4: 42

Narratives of Serious Adverse Experiences Reported or Updated During the SUR Period

Protocol 004

MK-400 mg b.i.d. Treatment Group

AN 12, a 56 year-old white male with a history of active Kaposi's sarcoma was randomized on Day 1 ([redacted]) to receive MK-0518 400 mg b.i.d. for 10 days of monotherapy. The patient entered the combination therapy phase on Day 100 ([redacted]), at which time tenofovir 300 mg q.d. and lamivudine 300 mg q.d. were added to the study regimen. On Day 409 ([redacted]), the patient experienced worsening Kaposi's sarcoma which resolved on Day 424 ([redacted]). The investigator determined Kaposi's sarcoma was definitely not related to study therapy.

Efavirenz 600 mg q.d. Treatment Group

AN 153, a 37-year-old Asian female with hyperlipidemia, post herpetic neuralgia, and a history of endometriosis and herpes zoster was randomized on Day 1 ([redacted]) to receive Efavirenz 600 mg q.d. plus tenofovir disoproxil fumarate 300 mg q.d. plus lamivudine 300 mg q.d. On Day 499 ([redacted]), the patient developed acute pharyngitis and was hospitalized. The patient was treated with acetaminophen 1000 mg, co-amoxiclav 1 gm b.i.d., bromhexine HCl 8 mg t.i.d., and codeine phosphate 10 mg t.i.d. On day 501 ([redacted]), the patient was discharged from the hospital and recovered on day 504 ([redacted]). The investigator determined acute pharyngitis was definitely not related to study therapy.

Protocol 005 Updates to WAES Reports discussed in Protocol 005 CSR

AN 3292, a 58-year-old white male with abdominal pain, cholestasis intrahepatic, lipodystrophy, diarrhea, eosinophilia, penicillin allergy, oral candidiasis, insomnia, hypercholesterolemia, and a history of drug-induced hepatitis, hemorrhoids, headache, vertigo, tendonitis, myocardial ischemia, and low back pain was randomized to receive placebo on Day 1 ([redacted]). The information presented here is in addition to that presented previously in PN005 CSR Section 14.4.3. On Day 344 ([redacted]) the patient switched to open-label MK-0518 400 mg b.i.d. in combination with emtricitabine (+) tenofovir disoproxil fumarate, enfuvirtide, lopinavir (+) ritonavir, and saquinavir mesylate. On Day 264 ([redacted]) of open-label therapy, the patient experienced anemia as a non-serious adverse experience and interrupted all study drug therapy including OBT. On the same day, the patient experienced a gastrointestinal hemorrhage and was hospitalized. The patient was started on sandostatin therapy and had a transfusion performed on Day 264 ([redacted]). An ECG and chest x-ray was

performed, showing normal results. An esogastroscopy performed on Day 265 ([redacted] 20[redacted]) showed esophagus varices. On Day 268 ([redacted] 20[redacted]) varices ligation was performed and study therapy was restarted on the same day. The patient was discharged and recovered from esophageal varices hemorrhage on Day 276 ([redacted] 20[redacted]). The investigator determined esophageal varices hemorrhage was probably not related to study drug therapy.

AN 3299, a 46-year-old White male with arthralgia, peripheral neuropathy, arthritis, dyspepsia, hyperlipidemia, diarrhea, avascular necrosis of bone, ongoing nausea, depressive disorder, and a history of poliomyelitis and abdominal tenderness, was randomized to receive 200 mg b.i.d. of MK-0518 on [redacted] 20[redacted] The information presented here is in addition to information presented previously in PN005 CSR section 14.4.1. On Day 392 ([redacted] 20[redacted]), the patient entered the open-label phase of the study and was placed on MK-0518 400 mg b.i.d in combination with ongoing OBT of zidovudine, ritonavir, indinavir sulfate, and emtricitabine. On Day 204 ([redacted] 20[redacted]) of open-label therapy, the patient was hospitalized with complaints of nausea, vomiting, some fever, chills, abdominal pain radiating to low back, and low urinary output. The patient had a lipase of 2557 IU/L (normal range: 1-100 IU/L) and amylase of 126 IU/L (normal range: 0-100 IU/L). The patient was diagnosed with acute pancreatitis and all antiretroviral therapy including study drug was held. On Day 207 ([redacted] 20[redacted]), the patient was discharged and considered recovered from acute pancreatitis. The investigator determined acute pancreatitis to be related to the patients' hyperlipidemic condition and probably not related to study drug therapy including OBT. At the time of the data freeze for this SUR, the serious adverse experience of rash as indicated in the attached WAES report was not entered into the database.

Protocol 005

Open-label MK-0518 400 mg b.i.d. plus OBT

AN 3294, a 37-year-old Asian male with AIDS, dermatitis, cataract and a history of hydronephrosis and peripheral sensory neuropathy was randomized on Day 1 ([redacted] 20[redacted]) to receive MK-0518 600 mg b.i.d. in combination with OBT of didanosine and lamivudine (+) zidovudine. Concomitant therapy included itraconazole and sulfamethoxazole (+) trimethoprim. On Day 383 ([redacted] 20[redacted]) the patient entered the open-label phase of the study and was placed on MK-0518 400 mg b.i.d. in combination with ongoing OBT. On Day 224 ([redacted] 20[redacted]) of open-label therapy the patient experienced decreased platelet count; his blood platelet count was 83000. On Day 242 ([redacted] 20[redacted]) of open-label therapy the patient was hospitalized for investigation of decreased platelet count. A bone marrow biopsy was performed on [redacted] 20[redacted] results showed normal cellular marrow with myelodysplasia likely secondary to retroviral disease. The patient was discharged from the hospital on [redacted] 20[redacted] with persisting decreased platelet count. The investigator determined that decreased platelet count was possibly related to study drug therapy in combination with OBT.

AN 3871, a 39-year-old White male with anxiety, fatigue, folliculitis, hyperlipidemia, overweight, rhinitis, tobacco abuse, and a history of osteonecrosis, influenza, liver disorder, hip arthroplasty, oral leukoplakia, seasonal allergy, and seborrheic dermatitis was randomized on Day 1 ([redacted]) to receive MK-0518 400 mg b.i.d. in combination with OBT of abacavir sulfate, atazanavir sulfate, didanosine, ritonavir, and tenofovir disoproxil fumarate. Concomitant therapy consisted of azelastine hydrochloride (+) benzalkonium chloride, lorazepam, and cetirizine hydrochloride. On Day 256 ([redacted]) the patient entered the open-label phase of the study and was placed on MK-0518 400 mg b.i.d. in combination with ongoing OBT. On Day 118 ([redacted]) of open-label therapy the patient was hospitalized for a hip joint cyst.. On Day 119 ([redacted]), the patient had a surgical operation to remove the cystic lesion from the hip joint. The patient was discharged and recovered on Day 120 ([redacted]). The investigator determined hip joint cyst to be definitely not related to study drug therapy.

Protocol 018 Updates to Previous Reports

MK-0518 Treatment Group

AN 7086, a 45-year-old White male with AIDS, polyneuropathy, hiatus hernia, genital warts, gastroenteritis, gastritis, bronchitis, onychomycosis, and a history of condyloma acuminatum, hepatitis B, herpes zoster, skin carcinoma, reflux esophagitis, pneumoocystis carinii pneumonia, oral candidiasis, esophageal ulcer, esophageal stenosis, esophageal candidiasis, mycobacterium tuberculosis, and lipodystrophy was randomized on Day 1 ([redacted]) to receive MK-0518 in combination with OBT of enfuvirtide, didanosine, efavirenz, and lopinavir (+) ritonavir. Concomitant therapy included omeprazole, sulfamethoxazole (+) trimethoprim, folic acid, and fluconazole. The information presented here is in addition to information presented previously in PN018 CSR section 14.4. On Day 211 ([redacted]), the patient was hospitalized for worsening gastritis. The patient received hydration, ranitidine, ciprofloxacin, dimenhydrinate, omeprazole, pantoprazole, metoclopramide, clonazepam, propionate (+) lysine chloridate, and meperidine hydrochloride. On Day 212 ([redacted]), the patient was improved and discharged on Day 214 ([redacted]). The investigator determined the worsening gastritis was probably related to study drug therapy including OBT.

AN 8241, a 43-year-old White female with AIDS, anemia, anicteric cholestasis, blindness in left eye, chronic rhinitis, cytomegalovirus retinitis, diarrhea, leukopenia, nausea, salivary hyposecretion, and a history of polyneuropathy, agranulocytosis, pneumoocystis carinii pneumonia, neuropathy peripheral, dermatitis, cryptococcosis, menometrorrhagia, myelodysplastic syndrome, bronchitis, and atypical mycobacterial infection was randomized to receive MK-0518 on Day 1 ([redacted]) in combination with OBT of atazanavir sulfate, darunavir, emtricitabine (+) tenofovir disoproxil fumarate, and ritonavir. Concomitant therapy included anethole trithione filgrastim, loperamide HCl, metoclopramide HCl, pantamide isethionate, valganciclovir HCl, and darbepoetin alfa. The information presented here is in addition to information presented

previously in PN018 CSR section 14.4. On Day 239 ([redacted]), hemoglobin for the patient was 6.4 g/dL (NR:11.5-16 g/dL), platelet count was 280000/mm^3 (NR: 150000-400000/mm^3), and white blood cell count was 8600/mm^3 (NR: 400-10000/mm^3). On Day 241 ([redacted]), the patient was hospitalized with a diagnosis of hemolytic anemia. Study drug therapy including OBT continued. While in the hospital a sputum culture on Day 240 ([redacted]) and a sputum exam on Day 241 ([redacted]) showed avium mycobacterium. Serum creatinine was normal; direct coombs test was positive (complement antibody = positive, IgG antibody = positive); serum parvovirus B19 was positive and PCR parvovirus was positive. A bone marrow exam performed on Day 241 ([redacted]) showed erythroblastic bone and signs of HIV myelodysplasia. The patient received infusions of immunoglobin and on Day 244 ([redacted]), the patient was discharged from the hospital with persisting hemolytic anemia. The patient was treated with amoxicillin and spiramycin for mycoplasma infection. At the time of the database freeze for this SUR, the patient had not recovered from this SAE. The investigator determined that hemolytic anemia was probably not related to study drug therapy including OBT.

There is additional information provided in the WAES database for this patient that is not included in the database freeze for this SUR: Day 260 ([redacted]), a sputum culture revealed avium mycobacterium. On Day 262 ([redacted]), the patient's blood hemoglobin was 7.1 g/dL (NR:11.5-16 g/dL) and on Day 262 and 263, the patient received immunoglobin IV. The blood hemoglobin was decreased to 5.7 g/dL (NR:11.5-16 g/dL) on Day 285 ([redacted]) and received packed red cells transfusion. That same day the patient had a positive parvovirus B19, cryoglobin test was positive and hepatitis C PCR was negative. On Day 288 ([redacted]), blood hemoglobin was 9.5 g/dL (NR:11.5-16 g/dL). On Day 290 ([redacted]), the patient returned to the hospital due to severe asthenia and severe dyspnea; at this time the blood hemoglobin was 4 g/dL (NR:11.5-16 g/dL). On day 292 ([redacted]), the patient was hospitalized and intravenous corticosteroid treatment was initiated. The patient still continued drug therapy including OBT. Hemolytic anemia was still persisting.

AN 8288, a 46-year-old white male with decreased CD4 lymphocytes, distal polyneuropathy, exercise-induced, asymptomatic increase of creatine phosphokinase, AIDS, depression, erectile dysfunction and a history of cryptococcosis and syphilis, was randomized on Day 1 ([redacted]) to receive MK-0518, 400 mg b.i.d. in combination with OBT of efavirenz, abacavir sulfate (+) lamivudine (KIVEXIA), and tenofovir disoproxil fumarate. On Day 30 ([redacted]), efavirenz was stopped due to depression. On an unknown date, the patient noticed an "abnormal feeling" (not further specified) and transient anal bleeding. Patient was hospitalized on Day 181 ([redacted]) for diagnostic work-up. Therapy with study medication continued. Histopathology results confirmed the diagnosis of anal carcinoma. Patient underwent a not further specified rectal surgery. On Day 195 ([redacted]), the patient was hospitalized for a second surgical treatment. The reporting investigator considered the anal carcinoma to be definitely not related to study therapy.

Placebo Treatment Group

AN 8234, a 42-year-old White male with AIDS, cytomegalovirus chorioretinitis, adrenal insufficiency, affect lability, epilepsy, vision blurred, post herpetic neuralgia, hepatitis C virus, smoker, and a history of cytomegalovirus infection, eczema, adrenocortical insufficiency acute, anal fissure, convulsion, meningoencephalitis herpetic, metabolic acidosis, molluscum contagiosum, mycobacterium kansasii infection, tuberculosis, oral candidiasis, rash, urinary tract infection enterococcal, polyneuropathy, pancytopenia, mediastinal mass, drug abuser, herpes zoster, cytomegalovirus chorioretinitis, and acute prerenal failure, was randomized on Day 1 ([redacted]) to receive placebo in combination with OBT of atazanavir sulfate, ritonavir, and emtricitabine (+) tenofovir disoproxil fumarate. Concomitant therapy included sulfamethoxazole (+) trimethoprim, valganciclovir HCl, and leucovorin calcium. The information presented here is in addition to information presented previously in PN018 CSR section 14.4. On Day 202 ([redacted]), the patient was hospitalized for epilepsy and fever. Study drug therapy continued. The patient was treated with valproic acid for epilepsy and acetaminophen for fever. The patient recovered from both epilepsy and fever and was discharged from the hospital on Day 232 ([redacted]). On Day 240 ([redacted]), the patient experienced productive cough, chest pain, and abdominal pain; the patient was admitted the same day with febrile syndrome. Study drug therapy continued. On Day 253 ([redacted]), the patient was discharged from the hospital considered recovered from febrile syndrome (recovered on Day 250 ([redacted]). On Day 257 ([redacted]), a culture of the portacatheter tip was positive for Staphylococcus epidermidis and a chest x-ray showed increased density in the base of right lung, identified as pneumonia. The patient was hospitalized for epilepsy, febrile syndrome, septic shock, and nosocomial pneumonia on Day 257 ([redacted]). The origin of the febrile syndrome was determined to be due to the infection in the catheter tip and the patient received vancomycin; imipenem was administered for 14 days for the treatment of the nosocomial pneumonia. The patient recovered from epilepsy ([redacted]), septic shock ([redacted]), and febrile syndrome ([redacted]). A chest x-ray performed on Day 267 ([redacted]) was normal and patient was considered recovered from nosocomial pneumonia the same day. While in the hospital the patient performed protocol visit 20 and switched to open-label therapy with an OBT regimen of enfuvirtide, darunavir, ritonavir, and lamivudine. The patient was discharged from the hospital on Day 278 ([redacted]). The investigator determined that fever, epilepsy (on [redacted] and [redacted]), febrile syndrome ([redacted] and [redacted]), septic shock, and nosocomial pneumonia were probably not related to study drug therapy including OBT.

The WAES reports also indicates a SAE of fever occurring on Day 286 ([redacted]). Due to the date of the database freeze for this SUR, this SAE of fever is not in the database.

Protocol 018

MK-0518 Treatment Group

AN 7019, a 45-year-old White male with AIDS, hepatitis C virus, HIV wasting syndrome, hepatic steatosis, hypertension, proteinuria, pyelonephritis, renal cyst, blood triglycerides increased and a history of cheilitis, asthenia, dermatitis, thrombophlebitis, sinusitis, relapsing fever, paraesthesia, esophageal candidiasis, mycobacterium avium complex infection, leukoplakia, drub abuser, herpes zoster ophthalmic, herpes zoster, and diarrhea was randomized on Day 1 ([redacted]) to receive MK-0518 400 mg b.i.d. in combination with OBT of enfuvirtide, ritonavir, and tipranavir and zidovudine. Concomitant therapy included nandrolone decanoate, pyrimethamine, and ramipril. On Day 208 ([redacted]), the patient was hospitalized for worsening nephrotic syndrome and underwent a renal biopsy on Day 209 ([redacted]). The renal biopsy revealed segmentary and focal glomerulosclerosis. The patient was discharged from the hospital on Day 209 with persisting nephrotic syndrome and focal glomerulosclerosis. The investigator determined that nephrotic syndrome and focal glomerulosclerosis was probably not related to study drug therapy including OBT.

AN 7067, a 44-year-old White male with AIDS, back pain, hepatitis C, and a history of anxiety, depression, hepatitis B, insomnia, pneumonia bacterial, oral candidiasis, esophageal candidiasis, mycobacterium tuberculosis, and a intravenous drug abuser was randomized on Day 1 ([redacted]) to receive MK-0518 in combination with OBT of abacavir sulfate, enfuvirtide, ritonavir, and tipranavir. No other concomitant therapy was taken at the time of this SAE. On Day 223 ([redacted]), the patient went to the hospital with complaints of upper respiratory tract cold, constipation, fever, and pain on right abdominal iliac fossa. An ultrasound performed that day revealed acute appendicitis and a biopsy the same day showed acute gangrenous appendicitis. The patient was hospitalized on Day 223 and an appendectomy was performed on Day 223. The patient interrupted study drug therapy on Day 223 ([redacted]) and restarted study drug therapy on Day 225 ([redacted]). The patient was discharged from the hospital on Day 226 ([redacted]) and recovered from appendicitis on Day 232 ([redacted]). The investigator determined that gangrenous appendicitis was definitely not related to study drug therapy including OBT.

AN 7123, a 56-year-old White male with HIV disease, lipodystrophy, psoriasis, leukopenia, hypertriglyceridemia, diarrhea, dermatitis, coronary artery disease, dyslipidemia, and a history of coronary disease, cytomegalovirus infection, diabetes mellitus, herpes zoster, molluscum contagiosum, mycobacterium kansasii infection, mycobacterium tuberculosis disseminated, neuropathy, and oral candidiasis was randomized on Day 1 ([redacted]) to receive MK-0518 in combination with OBT of enfuvirtide, ritonavir, saquinavir mesylate, and emtricitabine (+) tenofovir disoproxil fumarate. Concomitant therapy included ataranovir sulfamethoxazole (+) trimethoprim, folic acid, azithromycin, bisoprolol, hydrochlorothiazide (+) ramipril, valganciclovir HCl,

aspirin, granulocyte colony stimulating factor, and atorvastatin calcium. On Day 7 ([redacted]), the patient was hospitalized for worsening HIV disease. On Day 11 ([redacted]), the patient underwent computed axial tomography of the head and the abdomen; which revealed a micronodular enlargement of the omentum with signs of divarication of the mesenteric root. On Day 18 ([redacted]), the patient was placed on therapy with ciprofloxacin, ethambutol, and azithromycin. The patient recovered from worsening HIV disease and was discharged on Day 21 ([redacted]). The investigator determined that worsening HIV disease was definitely not related to study drug therapy including OBT.

AN 8250, a 51-year-old White male with AIDS, anemia, angiopathy, depression, diabetic neuropathy, diarrhea, goiter, osteoarthritis, headache, deafness, hepatic steatosis, hypertriglyceridemia, lipodystrophy, injection site reaction from enfuvirtide, shoulder pain, spinal disorder, splenomegaly, spinal osteoarthritis, diabetes mellitus, and a history of bronchitis, cholecystectomy, hemorrhoids, herpes zoster, hypertension, oral candidiasis, and pneumonia was randomized on Day 1 ([redacted]) to received MK-0518 in combination with OBT of emtricitabine (+) tenofovir disoproxil, saquinavir mesylate, and ritonavir. Concomitant therapy included ramipril, insulin lispro, biphasic isophane, loperamide HCl, insulin human, and insulin glargine. On Day 273 ([redacted]), the patient was hospitalized with chest pain without dyspnea. ECG revealed no ST-elevation, troponin T was negative and no diagnosis of myocardial infarction. Study drug therapy including OBT continued. The patient was diagnosed with musculoskeletal pain syndrome with chest pain as a symptom. Note: the SAE term in the CTS database at the time of the frozen file for this SUR is "chest pain". The patient recovered and was discharged. The investigator determined that musculoskeletal pain was probably not related to study drug therapy.

AN 8269, a 64-year-old Asian female with AIDS, creatine phosphokinase increased, hepatic function abnormal, hypertension, hypertriglyceridemia, oral candidiasis, , and a history of herpes zoster, mouth ulceration, and pneumoocystis carinii pneumonia, was randomized on Day 1 ([redacted]) to receive MK-0518 in combination with OBT of abacavir sulfate, didanosine, and lopinavir (+) ritonavir. Concomitant therapy included amlodipine besylate. On Day 222 ([redacted]), the patient was diagnosed with community-acquired pneumonia and was admitted to the hospital for intravenous antibiotic therapy of ampicillin (+) sulbactam sodium. On Day 224 ([redacted]), the patient started oral antibiotics of amoxicillin (+) clavulanate. The patient was discharged on Day 225 ([redacted]), considered recovered from community acquired-pneumonia. The investigator determined that community-acquired pneumonia was definitely not related to study drug therapy including OBT.

AN 8345, a 42-year-old white male with a nonspecified congenital renal anomaly, hepatosplenomegaly, lipodystrophy, a history of renal insufficiency, hepatitis B, hepatitis

C, esophageal candidiasis, PCP, and IV drug abuse, was randomized on [redacted] to the MK-0518 group. OBT included darunavir, emtricitabine (+) tenofovir and ritonavir. On Day 129 ([redacted]) the patient presented to an emergency room and was admitted on Day 130 ([redacted]). Pneumococcal pneumonia was diagnosed based on a chest x-ray and a blood culture that was positive for pneumococcus. Patient was also noted to have a serum creatinine of 285 µmol/L (3.22 mg/dL). The patient was diagnosed with pneumococcal pneumonia, acute on chronic renal insufficiency, and acute tubular necrosis. Pneumonia was treated with amoxicillin (+) clavulanate potassium initially, and then levofloxacin. The patient requested voluntary discharge. On Day 137 ([redacted]) a chest x-ray showed resolution of pneumonia. The investigator determined that pneumococcal pneumonia was definitely not related to study therapy and that the pneumococcal pneumonia had resolved. That same day the patient was re-hospitalized with acute on chronic renal insufficiency, and persistent acute tubular necrosis with serum creatinine of 356 µmol/L (4.03 mg/dL). All antiretroviral therapy was interrupted on Day 138 ([redacted]) and the patient was treated with IV hydration. Tenofovir was permanently discontinued and the patient restarted MK-0518 plus OBT (with the exception of tenofovir) on Day 150 ([redacted]). The reporting investigator considered the acute on chronic renal insufficiency and acute tubular necrosis to be definitely related to tenofovir. The patient recovered from acute on chronic renal insufficiency and acute tubular necrosis on Day 225 ([redacted]).

AN 8363, a 53-year-old White male with AIDS, dyslipidemia, hypertension, lipodystrophy, and a history of tobacco use, actinic keratosis, vasculitis cerebral, dry skin, chest pain, renal colic, mental disorder, ischemic cardiomyopathy, cerebellar syndrome, eczema, cheilitis, cerebral toxoplasmosis, cardiac failure, respiratory moniliasis, and angina unstable was randomized on Day 1 ([redacted]) to receive MK-0518 in combination with OBT of darunavir, emtricitabine (+) tenofovir disoproxil fumarate, ritonavir, and stavudine. Concomitant therapy included pravastatin calcium. On Day 128 ([redacted]), the patient went to the emergency room with severe chest pain. The EKG performed that day showed sinus rhythm, 65 per minute, normal axis, normal conduction intervals, narrow Q wave in D3 and aVF and prominent R since V1. Laboratory tests showed CPK 304 U (NR:not specified) with CPK isoenzyme MB 27 (NR:not specified) and troponin T inferior to 0.01. Six hours later CPK was 782 (NR:not specified) with CPK isoenzyme MB 102 and troponin T 0.393. The patient was admitted to the hospital and diagnosed with acute myocardial infarction. The patient was placed on therapy with enoxaparin, atenolol, aspirin, clopidogrel, and atorvastatin. Study drug therapy continued. On Day 130 ([redacted]), a cardiac catheterization was performed and showed: coronary common trunk with no lesions; anterior descending artery slightly calcified; proximal segment with permeable stent with minimum neointimal proliferation; medium segment with no lesions; distal segment with lesions of 50/55%. Circumflex artery: co-dominant vessel that is occluded in its proximal segment and the distal bed is lightly opaque due to homo-coronary circulation. Right coronary artery: co-dominant

vessel, its medium segment has a large and winding lesion with maximum narrow of 80% and it is small caliber vessel; another lesion of about 70% present before the origin of the posterior intraventricular. An angioplasty and stent placement was performed at the time of this cardiac catheterization. On Day 137 ([redacted]20[redacted], the patient recovered from acute myocardial infarction and was discharged from the hospital.

On Day 137 ([redacted]20[redacted], the same day patient was discharged for the acute myocardial infarction, the patient returned to the ER due to severe retro-sternal pain. Laboratory tests showed CPK 326 U (NR:not specified) with CPK isoenzyme MB 51 (NR:not specified) and troponin T 2.11. The patient was hospitalized with angina pectoris. Study drug therapy continued. On Day 140 ([redacted]20[redacted]), a catheterization was performed and showed: coronary common trunk with no lesions. Anterior descending artery: proximal segment with permeable stent; medium segment with no lesions; distal segment with lesions of 50 and 55%. Circumflex artery: co-dominant that is occluded in its proximal segment due to thrombosis of the stent. During this procedure, an angioplasty and dilation of stent were performed. On Day 148 ([redacted] 20[redacted]), the patient recovered from angina pectoris and was discharged. The investigator determined that both myocardial infarction and angina pectoris were disabling conditions that were probably not related to study drug therapy including OBT.

AN 8385, a 47-year-old Black male with hyperlipidemia, and a history of herpes simplex and sinusitis was randomized on Day 1 ([redacted]20[redacted]) to receive MK-0518 in combination with OBT of darunavir, delavirdine mesylate, emtricitabine (+) tenofovir disoproxil fumarate, and ritonavir. Concomitant therapy included fluconazole, sulfamethoxazole (+) trimethoprim, azithromycin, valacyclovir HCl, omega-3 marine triglycerides, ascorbic acid, and vitamin E. On Day 134 ([redacted]20[redacted], the patient experienced a reoccurrence of perianal herpes. On Day 155 ([redacted]20[redacted]), a culture from the anal lesion revealed methicillin-resistant staphylococcus aureus and on the same day viral polymerase chain reaction for herpes simplex virus, varicella virus, and cytomegalovirus detected herpes simplex virus II DNA. The patient received famciclovir for treatment of the HSV. On Day 162 ([redacted]20[redacted]), the patient was hospitalized; treatment with famciclovir was discontinued and treatment with intravenous acyclovir was initiated. At the time of the data freeze for this SUR; the patient was scheduled for a biopsy and excision of the perianal lesion on Day 177 ([redacted]20[redacted]; the perianal lesion was persisting. The investigator determined that perianal herpes simplex was possibly related to study drug therapy and possibly related to darunavir therapy.

AN 8391, a 48-year-old White male with AIDS, anal polyp, basal cell carcinoma, Bowen's disease, chronic diarrhea, folliculitis, foot drop, hepatomegaly, herpes genitalis, impotence, insomnia, lipodystrophy, lymphadenopathy, neuropathy peripheral, short-term memory loss, splenomegaly, testosterone low, thrombocytopenia, torn muscle, umbilical hernia, upper respiratory tract infection and a history of hepatitis B was randomized on Day 1 ([redacted]20[redacted]) to receive MK-0518 in combination with OBT of

darunavir, lamivudine, ritonavir, tenofovir disoproxil fumarate, and zidovudine. Concomitant therapy included betamethasone valerate, codeine phosphate, fluorouracil, imiquimod, nandrolone decanoate, pentamidine isethionate, psyllium husk, sildenafil citrate, valacyclovir HCl, vitamin B, and zolpidem tartrate. In [redacted] 20[redacted] prior to entry into the study, the patient had a computerized tomography scan that showed splenomegaly. On Day 93 ([redacted] 20[redacted], the patient was preparing to have elective surgical repair of an umbilical hernia and a computerized tomography scan of the abdomen showed splenomegaly and possible protal venous hypertension, which suggested an underlying hepatic disease as the etiology. On Day 123 ([redacted] 20[redacted]), an abdominal ultrasound was performed, which showed a degree of portal hypertension with splenomegaly and a slightly irregular liver, but with normal hepatopetal portal vein flow. On Day 129 ([redacted] 20[redacted]), the patient underwent an upper gastrointestinal endoscopy, which revealed esophageal varices protruding to at least a quarter of the lumen and of a tortuous nature at the lower end of the esophagus. Study therapy continued. On Day 164 ([redacted] 20[redacted]), the OBT therapy of zidovudine was discontinued and replaced by abacavir sulfate on Day 165. Esophageal varices were considered to be immediately life-threatening and portal hypertension was considered to be an other important medical event. At the time of the data freeze for this SUR, the patient has not recovered from protal hypertension and esophageal varices. The investigator determined esophageal varices to be definitely not related to study drug therapy including OBT and he determined portal hypertension to be probably not related to the use of study drug therapy including OBT.

OLPVF phase

AN 7024, a 57 year-old white male with a history of squamous cell carcinoma was randomized on Day 1 ([redacted] 20[redacted]) to receive placebo in combination with OBT of ritonavir, lamivudine, tipranavir, and enfuvirtide. On Day 118 ([redacted] 20[redacted], OBT therapy with tipranavir, ritonavir and enfuvirtide was discontinued. On Day 184 ([redacted] 20[redacted], the patient switched to MK-0518 400 mg b.i.d. post virologic failure and added darunavir to OBT and resumed therapy with ritonavir. On Day 94 of the open-label phase ([redacted] 20[redacted], the patient experienced recurrence of epidermoid carcinoma. Study therapy continued. The investigator determined that the recurrence of epidermoid carcinoma was probably not related to study therapy.

Placebo Treatment Group

AN 7045, a 45-year-old White male with erectile dysfunction, herpes simplex, lethargy, depression, hepatitis A, peripheral neuropathy, and a history of gall bladder disorder was randomized on Day 1 ([redacted] 20[redacted]) to receive placebo in combination with OBT of abacavir sulfate (+) lamivudine, darunavir, enfuvirtide, and ritonavir. Concomitant therapy included valacyclovir HCl and sildenafil citrate. On Day 269 ([redacted] 20[redacted]), the patient was hospitalized with oedema genital. Study drug therapy was not interrupted.

The patient was treated with intravenous antibiotics and paracetamol for pain relief. The patient recovered and was discharged from the hospital on Day 272 ([redacted]). The investigator determined that oedema genital was definitely not related to study drug therapy including OBT.

AN 7095, a 43-year-old White male with AIDS, HIV wasting syndrome, oral candidiasis, esophageal candidiasis, cerebral ataxia, chronic gastritis, dermatitis, encephalitis cytomegalovirus, epilepsy, onychomycosis, diarrhea, hemorrhoids, hemiparesis, lymphadenopathy, nausea, retinal degradation, erythema, musculoskeletal pain, oedema peripheral, skin papilloma, venous insufficiency, tinea barbae, skin hyperpigmentation, and a history of AIDS encephalopathy, abdominal colic, seroma, salmonella sepsis recurrent, psoriasis, status epilepticus, progressive multifocal leukoencephalopathy, pneumonia recurrent, pneumonia pneumococcal, bursitis, herpes zoster, gynaecomastia, mastectomy, erysipelas, dementia, cytomegalovirus infection, cerebral toxoplasmosis, and anemia was randomized on Day 1 ([redacted]) to receive placebo in combination with OBT of enfuvirtide, lamivudine, ritonavir, stavudine, tenofovir disoproxil fumarate, and tipranavir. Concomitant therapy included pyrimethamine, dapsone, leucovorin calcium, topiramate, valproate sodium, metoclopramide, fluconazole, loperamide HCl, nutritional supplements, betamethasone dipropionate (+) clotrimazole, polyvinyl alcohol, dexpanthenol, opium tincture, and triamcinolone acetonide. On Day 199 ([redacted]), laboratory analysis showed ALT 871 U/L (NR: not specified) and AST 417 U/L (NR: not specified). Due to these DAIDS grade 4 laboratory results, the investigator stopped tipranavir therapy. Study drug therapy with other OBT continued. The patient was hospitalized for further diagnostic workup to clarify these increased laboratory values. On Day 210 ([redacted]), the patient was diagnosed with toxic hepatitis due to tipranavir. On Day 211 ([redacted]), the patient was recovered and discharged from the hospital. The investigator determined that toxic hepatitis was definitely not related to study therapy and was definitely related to the use of tipranavir in the OBT.

AN 8215, a 43-year-old white male with AIDS, hyperhidrosis, lipodystrophy, libido decreased, lactose intolerance, depression, and a history of anorexia, aerophagia, arthralgia, asthma, cough, muscle spasms, dermatitis, eczema, gastroenteritis, alopecia, headache, dyspepsia, hepatomegaly, herpes virus infection, lip dry, lung infection, lymphadenopathy, flatulence, nausea, meteorism, personality disorder, neuropathy peripheral, pharyngitis, pollakiuria, pruritus, rhinitis, sleep disorder, and urinary tract infection was randomized on Day 1 ([redacted]) to receive placebo in combination with OBT of darunavir, emtricitabine (+) tenofovir disoproxil fumarate, and ritonavir. On Day 134 ([redacted]), the patient entered open-label post virologic failure and received MK-0518 400 mg b.i.d. in combination with ongoing OBT and the addition of enfuvirtide. Concomitant therapy included sulfamethizole (+) trimethoprim, sertraline HCl, and valacyclovir HCl. On Day 102 ([redacted]) of open-label therapy, the patient experienced right epididymitis, which was considered as a NSAE. The patient started treatment with amoxicillin (+) clavulanic acid on Day 112 ([redacted]). On

Day 122 ([redacted]20[redacted], an abdominal pelvic computed axial tomography was performed and showed a suspect epididymis abscess. The patient was hospitalized on Day 127 ([redacted]20[redacted]) to drain the abscess; however it was determined there was no abscess, but instead the presence of tumefaction. The patient discontinued treatment with amoxicillin (+) clavulanic acid and started ceftriaxone. On Day 133 ([redacted]20[redacted]), the patient was discharged from the hospital with persisting epididymitis and continued therapy with ceftriaxone. On Day 204 ([redacted]20[redacted]), the patient recovered from epididymitis. Study drug therapy including OBT was not interrupted during this SAE. The investigator determined that epididymitis was probably not related to study drug therapy including OBT.

AN 8228, a 44-year-old White male with AIDS, arthralgia, tinnitus, oral candidiasis, neuralgia, myalgia, lipohypertrophy, lipoatrophy, lactose intolerance, insomnia, proctitis herpes, gynaecomastia, fatigue, dry mouth, and diarrhea was randomized on Day 1 ([redacted]20[redacted]) to receive placebo in combination with OBT of darunavir, efavirenz, lamivudine, ritonavir, and tenofovir disoproxil fumarate. Concomitant therapy included acetaminophen, fluconazole, folic acid, hydroxocobalamin, ibuprofen, tramadol HCl, valacyclovir HCl, and zolpidem tartrate. On Day 272 ([redacted]20[redacted]), the patient experienced worsening gynaecomastia and was hospitalized on that day. The patient had a mammary reduction performed on Day 273 ([redacted]20[redacted]) and was considered recovered from worsening gynaecomastia at this time. The patient was discharged from the hospital on Day 274 ([redacted]20[redacted]). Study drug therapy continued. The investigator determined that worsening gynaecomastia was definitely not related to study drug therapy including OBT.

AN 8377, a 58-year-old White male with AIDS, back pain, depression, emphysema, fatigue, hypogonadism, weight decreased, and a history of arthralgia, benign parotid tumor, benign prostatic hyperplasia, fibromyalgia, esophageal candidiasis, pneumoocystis carinii pneumonia, pruritus, and syphilis was randomized on Day 1 ([redacted]20[redacted]) to receive placebo in combination with OBT of emtricitabine (+) tenofovir disoproxil fumarate, enfuvirtide, lamivudine (+) zidovudine, and lopinavir (+) ritonavir. Concomitant therapy included venlafaxine HCl, testosterone, calcium carbonate, albuterol, oxycodone HCl, acetaminophen (+) codeine phosphate, tiotropium, ciclesonide, lumiracoxib, ergocalciferol, paracetamol, domperidone, lactulose, lorazepam, and protein. On Day 148 ([redacted]20[redacted]), the patient was hospitalized for malnutrition (onset was Day 135 ([redacted]20[redacted]); which was considered to be due to panic attacks and poor sleep. Study drug therapy continued. The patient received enteral feedings while hospitalized and instruction on panic attacks and breathing techniques. The patient was improving by Day 154 ([redacted]20[redacted]) and was discharged from the hospital on Day 161 ([redacted]20[redacted]) with persisting panic attacks, malnutrition, and poor sleep. At the time of the database freeze for this report, the patient was not recovered from panic attacks, malnutrition, and poor sleep. The investigator determined that malnutrition, panic attacks, and poor sleep were probably not related to study drug therapy including OBT.

AN 8402, a 43-year-old White male with AIDS, depression, and a history of cryptococcosis, herpes zoster, mycobacterium tuberculosis, and syphilis was randomized on Day 1 ([redacted]) to receive placebo in combination with OBT of emtricitabine, ritonavir, tenofovir disoproxil, and tipranavir. Concomitant therapy included clonazepam, gabapentin, paroxetine, and sulfamethoxazole (+) trimethoprim. The patient experienced worsening depression on Day 81 ([redacted]) and stopped all study therapy; did not return for study visits and started to abuse cocaine. On Day 105 ([redacted]), the patient was hospitalized for worsening depression. The patient started therapy with mirtazapine, clonazepam, and risperidone. On Day 112 ([redacted]), the patient restarted study drug therapy including OBT. The patient recovered from worsening depression and was discharged on Day 112. The investigator determined that worsening depression was probably not related to study drug therapy including OBT.

On Day 158 ([redacted]), the patient was hospitalized due to an intentional overdose of psychotic drugs. On Day 162 ([redacted]), the patient was discharged from the hospital and recovered from the intentional overdose. Study drug therapy including OBT continued. The investigator determined the intentional overdose to be probably not related to study drug therapy including OBT.

Protocol 019 Updates to Previous Reports

MK-0518 Treatment Group

AN 16347, a 49-year-old White male with pericarditis, hypertension, hyperlipidemia, herpes simplex, folliculitis, fatigue, depression, deep vein thrombosis, anxiety, diarrhea, cytomegalovirus retinitis, allodynia, candidiasis, chronic obstructive pulmonary disease, coronary artery disease, gastroesophageal reflux disease, squamous cell carcinoma, smoker, sinusitis, lipoatrophy, neuropathy peripheral, and a history of pneumonia, Kaposi's sarcoma, nephrolithiasis, syphilis, retinal detachment, wasting, AIDS class III, night sweats, intermittent pyrexia, and somnolence was randomized on Day 1 ([redacted]) to receive MK-0518 in combination with OBT of tipranavir, emtricitabine (+) tenofovir disoproxil fumarate, and ritonavir. The information presented here is in addition to information presented previously in PN019 CSR section 14.4. The patient recovered from pneumonia and DVT previously reported as ongoing; however the patient did not recover from esophageal candidiasis at the time of this data freeze. Study drug therapy including OBT was restarted on Day 110 ([redacted]). The patient was again admitted to the hospital on Day 189 ([redacted]) for evaluation and treatment of pneumonia based on dyspnea. Treatment with levofloxacin, vancomycin, and piperacillin sodium (+) tazobactam sodium was started and continued at the time of this data freeze. The patient was discharged on Day 197 ([redacted]) and pneumonia resolved at an unknown date in February. The investigator determined that this episode of pneumonia was definitely not related to study drug therapy including OBT.

The WAES report attached also reports a serious AE of pneumonia occurring on Day 221 ([redacted]); this SAE is not included in the current data freeze for this SUR.

Placebo Group

AN 16231, a 18-year-old Black male with neutropenia, asthma, salmonella infection, lymphadenopathy, intermittent urinary tract infections, splenomegaly, cardiomegaly, and a history of pericardial effusion, leukopenia, intermittent anemia, disseminated cryptococcosis and gastroenteritis, was randomized on Day 1 ([redacted]20[redacted]) to receive placebo in combination with OBT. On Day 129 ([redacted]20[redacted]), the patient switched to open-label MK-0518 400 mg b.i.d. due to virologic failure on blinded therapy. OBT consisted of abacavir sulfate (+) lamivudine, atazanavir sulfate, didanosine, and zidovudine. The information presented here is in addition to information presented previously in PN019 CSR section 14.4. On Day 132 ([redacted]20[redacted]) of open-label post virologic failure therapy, the patient was hospitalized with gastroenteritis. The patient had increased stools the day prior to admission without bleeding. Blood and stool cultures were collected at admission with results not available as of this data freeze. The patient received intravenous fluids and ciprofloxacin HCl. Study therapy continued during this serious adverse experience. The patient recovered and was discharged from the hospital on Day 136 ([redacted]20[redacted]). The investigator determined that gastroenteritis was definitely not related to study drug therapy including OBT.

There are additional serious adverse experiences (worsening salmonella gastroenteritis on Day 194 ([redacted]20[redacted]) and weight decreased post discontinuation from the study due to lack of efficacy) in the attached NWAES report; however due to the time of the database freeze for this SUR these serious adverse events were not included in the database freeze.

Protocol 019

MK-0518 Treatment Group

AN 14404, a 31-year-old Hispanic male with AIDS, injection site nodules, injection site erythema, genital wart, and a history of liver abscess, cerebral toxoplasmosis, and herpes genitalis was randomized on Day 1 ([redacted]20[redacted]) to receive MK-0518 in combination with OBT of enfuvirtide, lamivudine, and lopinavir (+) ritonavir. On Day 182 ([redacted]20[redacted]), the patient was hospitalized for acute diarrhea with abdominal distension secondary to adynamic ileus and hypokalemia secondary to the diarrhea. Parenteral hydration was given along with buscapine for abdominal pain, ranitidine for gastric protection, and potassium for hypokalemia. The patient's serum potassium was 3.3.mMol/L (normal range: 3.6-5 mMol/L) on Day 183 ([redacted]20[redacted]) and 3.62 mMol/L on Day 184 ([redacted]20[redacted]). Study drug therapy including OBT was interrupted for two days and resumed on Day 185 ([redacted]20[redacted]); due to the date of the data freeze for this SUR the study drug information is not provided in the database data. On Day 185 ([redacted]20[redacted]), the patient recovered from acute diarrhea and was discharged from the hospital (the same day). The investigator determined the acute diarrhea to be probably not related to study drug therapy including OBT.

AN 14405, a 59-year-old Hispanic male with AIDS, basal cell carcinoma, hypertensive cardiomyopathy, hypertension, diabetes mellitus, lipohypertrophy, fat atrophy, neuralgia, obesity, sleep disorder, and a history of depression was randomized on Day 1 ([redacted] 20[redacted]) to receive MK-0518 in combination with OBT of atazanavir sulfate, lopinavir (+) ritonavir, and enfuvirtide. Concomitant therapy consisted of doxepin HCl and glyburide. On Day 149 ([redacted] 20[redacted]), the patient experienced headaches and dizziness. On Day 153 ([redacted] 20[redacted]), the patient interrupted study drug therapy and presented at the emergency room. A computed axial tomography performed on Day 153, showed a quistic lesion previously known to this patient and a cerebrospinal fluid analysis performed the same day reported an increase in lymphocyte count. The patient was diagnosed with cluster migraine and hospitalized on Day 153. Treatment with valproic acid and naproxen was started. The patient recovered and was discharged on Day 158 ([redacted] 20[redacted]). The investigator determined cluster migraine to be probably not related to study drug therapy including OBT.

AN 15082, a 45-year-old Black male with AIDS, HIV wasting, convulsion disorder, hypercholesterolemia, and a history of facial wasting, rash, hypertriglyceridemia, and epilepsy was randomized on Day 1 ([redacted] 20[redacted]) to receive MK-0518 in combination with OBT of tipranavir, ritonavir, enfuvirtide, emtricitabine (+) tenofovir disoproxil fumarate (started on [redacted] 20[redacted]). Concomitant therapy included gabapentin, lamotrigine, atorvastatin calcium, and testosterone. On Day 202 ([redacted] 20[redacted]), the patient experienced a seizure and was admitted to the hospital overnight. The patient was already taking medication to control seizures. The patient recovered from the seizure. The investigator determined that seizure was definitely not due to study drug therapy including OBT. At the time of the data freeze for this SUR, information regarding procedures performed at the hospital and treatment received during hospitalization had not been received from the investigative site.

AN 15090, a 45-year-old white male with adrenal cortical insufficiency, bilateral temporal wasting, pain in leg, AIDS, cryptosporidiosis, Kaposi's sarcoma, drug hypersensitivity to antibiotics, cytomegalovirus retinitis, and a history of neutropenia, anemia, arterial thrombosis, hypogonadism, anxiety, depression, cryptococcosis, extrapulmonary, and mycobacterium avium complex infection was randomized on Day 1 ([redacted] 20[redacted]) to receive MK-0518, 400 mg b.i.d. in combination with OBT of emtricitabine (+) tenofovir disoproxil fumarate, darunavir, ritonavir, enfuvirtide, and etravirine. On Day 52 ([redacted] 20[redacted]), the patient was hospitalized for progressive diarrhea and weight loss. Diagnostic work-up revealed cytomegalovirus colitis. Study therapy continued. The reporting investigator considered the cytomegalovirus colitis to be definitely not related to study therapy. Patient was hospitalized on Day 100 ([redacted] 20[redacted]) due to pneumonia. Invasive aspergillosis of the lung was diagnosed by a bronchoscopy and confirmed on pathology. Patient was diagnosed with E. coli and klebsiella pneumonia. Also observed was rapid wasting syndrome. Progressive Kaposi's sarcoma of the lower extremities was suspected but not found in the lung or bronchioles.

These events were considered not related to study drug by the reporting investigator. On Day 179 ([redacted]), there was an initial report of squamous cell cancer of the right temple, which was growing. This was diagnosed on Day 140 ([redacted]) on biopsy. Mohs surgery was performed and patient was diagnosed with increasing submandibular lymph node involvement. A radical neck dissection took place on Day 179 ([redacted]). The event of squamous cell carcinoma was subsequently updated to metastatic squamous cell carcinoma. The reporting investigator determined that squamous cell carcinoma was not related to study therapy.

AN 15113, a 42-year-old Black male with AIDS, wrist fracture, rectal lesion, rash vesicular, lipodystrophy, insomnia, iodine allergy, diarrhea, asthma, fungal rash, lactose intolerance, papilloma viral infection, and pollakiuria, and a history of bronchitis, sinusitis, nausea, pancreatitis, and gastroenteritis cryptosporidial was randomized on Day 1 ([redacted]) to receive MK-0518 in combination with OBT of darunavir, enfuvirtide, ritonavir, and emtricitabine (+) tenofovir disoproxil fumarate. Other concomitant therapy included loperamide HCl, ibuprofen, loratadine (+) pseudoephedrine sulfate, triamcinolone acetonide, trazodone HCl, and valacyclovir HCl. The patient experienced a mass on buttocks on Day 30 ([redacted]) and was continually reminded to pursue further evaluation. On Day 119 ([redacted]), the patient noticed a tag in the buttock region occasionally bleeding; the patient was referred to a colorectal surgeon who performed a biopsy and excision. The biopsy showed squamous mucosa with severe dysplasia carcinoma in situ with extension to the ink margin. On Day 163 ([redacted]), the patient had an anal condyloma excised; biopsy results showed squamous mucosa with severe dysplasia carcinoma in situ with extension to the ink margin marked HPV cytopathic effect present. The investigator determined the mass on buttocks and anal condyloma to be probably not related to study drug therapy including OBT. The investigator considers it to be possible that the improved immune status of the patient on the study may have contributed to the inflammation and the lesions.

AN 16248, a 41-year-old White male with diarrhea, increased appetite, herpes simplex, cough, fatigue, headache, and a history of anogenital warts, tongue neoplasm, sinusitis, anal fistula, candidiasis, glossitis, and post concussion syndrome was randomized on Day 1 ([redacted]) to receive MK-0518 in combination with OBT of ritonavir, tipranavir, and emtricitabine (+) tenofovir disoproxil fumarate. Concomitant therapy included sulfamethoxazole (+) trimethoprim, azithromycin, dronabinol, and famciclovir. On Day 225 ([redacted]), the patient was admitted to the hospital for evaluation of moderate abdominal pain. Study drug therapy and OBT continued. Abdominal pain resolved on Day 257 ([redacted]). At the time of the data freeze for this SUR the date of discharge from the hospital was not provided. The investigator determined that abdominal pain was definitely not related to study drug therapy including OBT.

AN 16279, a 48-year-old black male with esophageal candidiasis, pneumoocystis carinii pneumonia, pharynx discomfort, chronic back pain, chronic sinusitis, depression, diarrhea, fatigue, gingival disorder, gout, hay fever, hypertension, induration, lipodystrophy, nausea, neuropathy peripheral, perianal herpes simplex, psoriasis, tooth pain, and a history of toxoplasmosis, pneumothorax, insomnia, cardiac flutter, anemia, anxiety, abdominal bloating, cellulitis of leg, chest pain, conjunctivitis, chronic cough, HIV wasting syndrome, tinea pedis, and vomiting was randomized on Day 1 ([redacted] 20[redacted]) to receive MK-0518 in combination with OBT of abacavir sulfate (+) lamivudine, tenofovir disoproxil, and tipranavir. On Day 168 ([redacted] 20[redacted]), the patient entered the open-label post virologic failure and was placed on MK-0518 400 mg b.i.d. in combination with ongoing OBT. Concomitant therapy included mometasone furoate, ibuprofen, valacyclovir HCl, atovaquone, lansoprazole, ramipril, bupropion HCl, hydrochlorothiazide, montelukast sodium, voriconazole, omega-3 marine triglycerides, pentamidine isethionate, colchicine, metronidazole, vitamin E, and acetaminophen (+) hydrocodone bitartrate. On Day 57 ([redacted] 20[redacted]) of the open-label therapy, the patient experienced esophageal candidiasis of moderate intensity and interrupted study drug therapy on Day 73 ([redacted] 20[redacted]). The patient was hospitalized on Day 76 ([redacted] 20[redacted]) for worsening esophageal candidiasis. While hospitalized, the patient was diagnosed with pneumoocystis carinii pneumonia; this was considered as an event of clinical interest. The patient received intravenous amphotericin while hospitalized. On Day 80 ([redacted] 20[redacted]), the patient restarted OBT regimen of abacavir sulfate (+) lamivudine, darunavir, emtricitabine, ritonavir, and tenofovir disoproxil. The patient was discharged from the hospital on Day 91 ([redacted] 20[redacted]) recovered from esophageal candidiasis and study drug therapy (MK-0518) was restarted on the same day. The investigator determined esophageal candidiasis to be definitely not related to study drug therapy including OBT.

At the time of the data freeze for this SUR; the information in the database for this SAE has the term indicated as pneumoocystis carinii pneumonia. The narrative listed here is based on the WAES information attached since the report has the most recent information.

Placebo Group

AN 15046, a 50-year-old White male with AIDS, hypercholesterolemia, lipodystrophy, hypertriglyceridemia, sore throat, left eye chronic disease, cerebral after effect post trauma, induration on right and left legs due to enfuvirtide injections, penicillin allergy, sulfonamide allergy, and a history of pneumoocystis carinii pneumonia, esophageal candidiasis, otitis, depression, condyloma, urogenital herpes recurrent, rash due to cephalexin, allergic reaction to antibiotics, aggressive behavior, anxiety, polyneuritis, and herpes zoster was randomized on Day 1 ([redacted] 20[redacted]) to receive placebo in combination with OBT of enfuvirtide, tenofovir disoproxil fumarate, atazanavir sulfate, ritonavir, and lamivudine. On Day 127 ([redacted] 20[redacted]), the patient switched to open-label

MK-0518 400 mg b.i.d. in combination with ongoing OBT; this change was due to lack of efficacy on blinded therapy. Concomitant therapy included atorvastatin calcium, atovaquone, famciclovir, fluconazole, and venlafaxine HCl. On Day 113 ([redacted]) of open-label therapy, the patient experienced severe depression. Severe depression was considered to be an other important medical event by the investigator. The patient had interrupted all study drug therapy on his own accord two days prior to presentation of the severe depression. On Day 113, therapy with venlafaxine HCl was discontinued and on Day 114 ([redacted]), the patient started therapy with citalopram hydrobromide. Study therapy including OBT drugs continued during this SAE. On Day 169 ([redacted]), the patient recovered from depression. The investigator determined that severe depression was possibly related to study drug therapy including OBT.

AN 15125, a 59-year-old White male with cough, and sinusitis was randomized on Day 1 ([redacted]) to receive placebo in combination with OBT of enfuvirtide, lamivudine, ritonavir, saquinavir, and tenofovir disoproxil fumarate. Other concomitant therapy included acetylcysteine, azithromycin, and amoxicillin (+) clavulanate potassium. The patient had been having fevers twice a day since Day 131 ([redacted]) and took dipyrone to treat the fevers. On Day 164 ([redacted]), the patient experienced 3.82% neutrophil count (NR: 45-75%) and white blood cell count of 580/mm^3 (NR: 3600 - 11000 /mm^3) and subsequently was hospitalized for treatment of this life-threatening condition. The patient received cefepime in the hospital to treat neutropenia, which resolved on Day 169 ([redacted]). On Day 174 ([redacted]), the patient had an echocardiogram performed, which showed endocarditis and an aortic vegetation on the ventricular side. Vancomycin and gentamycin were started on Day 175 ([redacted]). Study drug therapy continued. On Day 184 ([redacted]), the patient experienced renal failure and on Day 185 ([redacted]) gentamycin was discontinued. All study drug therapy was interrupted on Day 187 ([redacted]) since the patient's condition was not improving. On Day 197 ([redacted]), the patient was discharged from the hospital. The patient had another echocardiogram performed on Day 220 ([redacted]), which showed calcified lesions on the aortic valve. Endocarditis resolved on Day 226 ([redacted]) and renal failure resolved on Day 229 ([redacted]). The patient restarted all study drug therapy including OBT on Day 233 ([redacted]). The investigator determined that neutrophil count decreased and endocarditis were probably not related to study drug therapy including OBT; renal failure was probably related to the use of tenofovir disoproxil fumarate and gentamycin.

The WAES report also indicates a SAE of fever on Day 246 ([redacted]); this SAE is not in the data freeze for this SUR.

AN 16346, a 70-year-old White male with AIDS, chronic obstruction pulmonary disease (COPD), neuropathy peripheral, diabetes mellitus, insomnia, irritable bowel syndrome, back pain, lipoatrophy, headache, diarrhea, candidiasis, abdominal pain, depression, fatigue, HIV wasting syndrome, hypogonadism, seborrhea, and a history of

pneumoocystis carinii pneumonia, bronchitis acute, memory disturbance, epistaxis, lymphadenopathy, proctitis, syphilis, tinea cruris, macrocytosis, and cataract was randomized on Day 1 ([redacted]20[redacted]) to receive placebo in combination with OBT of darunavir, ritonavir, and emtricitabine (+) tenofovir disoproxil fumarate. Other concomitant therapy included simethicone, metronidazole, albuterol sulfate (+) ipratropium bromide, budesonide, propantheline bromide, sertraline HCl, testosterone, and alpha galactosidase A. On Day 139 ([redacted]20[redacted]), the patient was hospitalized for pneumonia. A chest x-ray performed on Day 139 showed right lower lobe infiltrate. The patient had experienced a myocardial infarction (considered to be a NSAE) prior to his admission for pneumonia. Study drug therapy was interrupted for seven days. The patient recovered from pneumonia and was discharged on Day 155 ([redacted]20[redacted]). The investigator determined that pneumonia was definitely not related to study drug therapy including OBT.

On Day 212 ([redacted]20[redacted]), the patient experienced worsening of his chronic diarrhea and began treatment for clostridium difficile colitis. On Day 220 ([redacted]20[redacted]), the patient was admitted to the hospital for clostridium difficile colitis. On admission he was found to have an abnormal computed axial tomography; showing extensive colon wall thickening with pericolonic edema consistent with pan colitis, infection versus inflammation, versus ischemia. A small amount of intraabdominal ascites was present. On Day 221 ([redacted]20[redacted]), the patient had an abnormal white blood cell count of 14.17 x 10^3/uL (normal range:3.8-10.7 x 10^3/uL). The patient had been receiving treatment with vancomycin orally for 7 days prior to his admission; this treatment was stopped on Day 221 ([redacted]20[redacted]) and treatment with piperacillin (+) tazobactam and metronidazole was started. A head computed axial tomography performed on Day 221 ([redacted]20[redacted]), showed an cerebral infarction in the left occipital lobe, which was considered to be disabling. At the time of the data freeze for this SUR, the patient had not recovered from either clostridium difficile colitis or cerebral infarction. The investigator determined that clostridium difficile colitis and cerebral infarction were definitely not related to study drug therapy including OBT.

Additional patient narratives were provided to FDA previously as a result of specific FDA queries. If not provided above, the narratives are provided here for completeness:

<u>Protocol 004 - MK-0518 400 mg b.i.d. group</u>

AN 165, a 34 year-old white male with a history of active Kaposi's sarcoma was randomized in Part II (combination therapy phase) ([redacted]20[redacted]) to receive MK-0518 400 mg b.i.d. plus tenofovir 300 mg q.d. plus lamivudine 300 mg q.d. On Day 181, the patient experienced Kaposi's sarcoma which was not indicated as a worsening of the pre-existing condition. The investigator determined that Kaposi's sarcoma was definitely not related to study therapy. Subsequently, during data review post submission of this application, the investigator determined that Kaposi's sarcoma on Day 181 did not represent a serious adverse experience since this did not represent a worsening of the pre-existing condition.

Protocol 018 - MK-0518 400 mg b.i.d. group

AN 7036, a 54 year old white male with HIV infection, CD4 lymphocytes decreased, acquired immunodeficiency syndrome, Kaposi's sarcoma AIDS related, and prostatic hypertrophy was randomized on [redacted] (Day 1) to MK-0518 in combination with optimized background therapy of ritonavir, darunavir, emtricitabine (+) tenofovir disoproxil fumarate, and enfuvirtide. Concomitant therapy included sulfamethoxazole (+) trimethoprim, fluconazole, and vitamins (unspecified). The absolute neutrophil count (ANC) at screening (Day -44) was 0.75 10[3]/microL, and at randomization it was 0.77 10[3]/microL.

On Day 27 ([redacted]) patient experienced decreased ANC of 0.32 10[3]/microL. The patient was considered to be well clinically. On Day 34 ([redacted]), the ANC decreased further to 0.12 10[3]/microL. On Day 36 ([redacted]), due to these laboratory results, all antiretroviral treatment was interrupted and sulfamethoxazole (+) trimethoprim and fluconazole were discontinued. On Day 37 ([redacted]) ANC was 0.53 10[3]/microL and on Day 40 ([redacted]) it was 1.73 10[3]/microL. On Day 42 ([redacted]), the patient re-started treatment with MK 0518 400 mg, darunavir, ritonavir, emtricitabine (+) tenofovir disoproxil fumarate, and enfuvirtide. The SAE did not reappear after restarting test drug, on Day 43 ([redacted]) the ANC was 2.07 10[3]/microL and the investigator considered the adverse experience of absolute neutrophil count decreased to have resolved. The decreased ANC was considered to be an "other important medical event" and was considered probably not related to study drug.

On Day 108 ([redacted]) the patient experienced common cold and expectoration (both NSAEs). Symptoms recovered without treatment. On Day 111 ([redacted]) CD4 cell count was 128 and HIV-RNA level was 68 copies/ml. On Day 118 ([redacted]) the patient experienced febrilia which continued for two weeks. The patient also had symptoms of a urinary tract infection and a cough with minimal expectoration. On Day 128 ([redacted]) the patient was hospitalized due to pneumonia. A urine culture was performed and the result was negative. Blood samples showed: WBC: 6.2, neutrophil count 4.84, CRP: 95. Arterial blood gas showed: PH 7.46, hydrogen carbonate 27, PCO_2 5.0, PO_2 9.4, and whole blood deoxyhemoglobin test 0.95. Chest x-ray performed that same day showed suspected PCP infiltration. Naso-tracheal aspirate showed: microscopy for Mycobacteria was negative; microscopy and culture were negative (no alpha hemolytic streptococcus in final result); PCR for *Legionella pneumophila* was negative; PCRs for *Chlamydia pneumoniae* and *Chlamydia psittaci* were negative; PCR for *Mycoplasma pneumoniae* was negative; PCR for *Pneumocystis carinii* was negative. Bronchoscopy was not performed. On Day 129 ([redacted]) blood gas test was performed again showing: PH 7.46; hydrogen carbonate 27; P CO_2 4.9; HB-O 0.95. The patient started treatment with sulfamethoxazole (+) trimethoprim on Day 129. On Day 131 penicillin (unspecified) therapy (8 mIU) was started. PCP

diagnosis was rejected. On Day 134 ([redacted]) the patient recovered from pneumonia. Sulfamethoxazole (+) trimethoprim was discontinued, and the patient was discharged from the hospital. That same day the penicillin V (2.4 gr/day) was started until Day 143 ([redacted]) and the patient continued to be well. Study therapy was not interrupted and the investigator felt that pneumonia was definitely not related to study therapy.

AN 8287, a 61 year old female with AIDS, decreased CD4 count, diarrhoea and Hodgkin's lymphoma and a history of a herniated disc, hysterectomy, cachexia, genital herpes, drug intolerance and oesophageal candidiasis was randomized on [redacted] (Day 1) to receive MK-0518 (400 mg, twice a day). Optimized background therapy included saquinavir, ritonavir, abacavir sulfate (+) lamivudine, and stavudine. Concomitant therapy included loperamide HCl. On Day 15 ([redacted]) the patient came to the investigator's office for protocol visit 3 and reported running out of study medication. The investigator realized that the patient had been taking incorrect doses of study medication. From Day 1 ([redacted]) to Day 14 ([redacted]), the patient took by mistake 2 tablets BID of MK-0518 (1,600 mg/day). The patient was clinically asymptomatic, and did not experience any adverse events as a result of taking the incorrect study dose. Subsequently therapy with the prescribed dose of MK-0518, 1 tablet twice a day (800 mg/day) was initiated. The reporting investigator felt that the overdose was definitively not related to study therapy.

Protocol 019 - OLPVF phase

AN 16237, a 41-year-old Black female with HIV infection, CD4 lymphocytes decreased, AIDS, cryptosporidial gastroenteritis, cytomegalovirus chorioretinitis, depression, and drug hypersensitivity, was randomized on Day 1 to receive placebo in combination with an OBT of tipranavir, ritonavir, stavudine, and lamivudine. Concomitant therapy included sulfamethoxazole (+) trimethoprim, opium, paromomycin, ethionamide, fluconazole, azithromycin, valacyclovir hydrochloride, and atropine sulfate (+) diphenoxylate hydrochloride. On Day 66, the patient was admitted to the hospital for dehydration, which was secondary to a worsening of cryptosporidial gastroenteritis, which was treated with imipramine hydrochloride. On Day 70, the patient was diagnosed with a worsening of cytomegalovirus retinitis, which prolonged the patient's hospitalization. The patient was treated with ganciclovir sodium. On Day 72, the patient recovered from of cryptosporidial gastroenteritis and was discharged from the hospital. On Day 89, the patient discontinued ganciclovir sodium and began therapy with valganciclovir hydrochloride. On Day 110, the patient was hospitalized for pneumonia. On Day 111, a bronchoscopy ruled out *Pneumoocystis carinii* and revealed *Staphylococcus aureus*. The patient began treatment with moxifloxacin hydrochloride and sulfamethoxazole (+) trimethoprim. On Day 112, the patient was discharged from the hospital. On Day 118, the patient recovered from pneumonia but was diagnosed with a recurrence of worsening cryptosporidial gastroenteritis. On Day 127, the patient was

switched to open-label MK-0518 treatment. From Day 152 to Day 174, study drug and OBT were interrupted due a nonserious adverse experience of cholecystitis acute and failure to thrive. On Day 166, the patient was admitted to the hospital for failure to thrive. On Day 187, the patient recovered from worsening cryptosporidial gastroenteritis; however, the patient has not recovered from failure to thrive. The investigator determined that the cryptosporidial gastroenteritis, cytomegalovirus retinitis, pneumonia, recurrence of cryptosporidial gastroenteritis, and failure to thrive were definitely not related to study drug.

Appendix 2.7.4: 43

Number (%) of Patients With Specific Serious Clinical Adverse Experiences (Incidence >0% in One or More Treatment Groups) by System Organ Class - (Protocol 005: Substudies A and B Combined Entire Study Period) - *Cumulative Data*

	MK-0518 200 mg b.i.d. (N = 43)		MK-0518 400 mg b.i.d. (N = 45)		MK-0518 600 mg b.i.d. (N = 45)		Placebo (N = 45)		Total (N = 178)	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Patients With One Or More Adverse Experiences	4	(9.3)	8	(17.8)	4	(8.9)	3	(6.7)	19	(10.7)
Patients With No Adverse Experience	39	(90.7)	37	(82.2)	41	(91.1)	42	(93.3)	159	(89.3)
Blood And Lymphatic System Disorders	1	(2.3)	0	(0.0)	1	(2.2)	0	(0.0)	2	(1.1)
Anaemia	0	(0.0)	0	(0.0)	1	(2.2)	0	(0.0)	1	(0.6)
Lymphadenopathy	1	(2.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.6)
Cardiac Disorders	0	(0.0)	1	(2.2)	1	(2.2)	0	(0.0)	2	(1.1)
Acute Myocardial Infarction	0	(0.0)	1	(2.2)	0	(0.0)	0	(0.0)	1	(0.6)
Bradycardia	0	(0.0)	0	(0.0)	1	(2.2)	0	(0.0)	1	(0.6)
Cardio-Respiratory Arrest	0	(0.0)	0	(0.0)	1	(2.2)	0	(0.0)	1	(0.6)
Coronary Artery Disease	0	(0.0)	1	(2.2)	0	(0.0)	0	(0.0)	1	(0.6)
Gastrointestinal Disorders	1	(2.3)	1	(2.2)	0	(0.0)	0	(0.0)	2	(1.1)
Irritable Bowel Syndrome	0	(0.0)	1	(2.2)	0	(0.0)	0	(0.0)	1	(0.6)
Pancreatitis Acute	1	(2.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.6)
General Disorders And Administration Site Conditions	0	(0.0)	0	(0.0)	1	(2.2)	0	(0.0)	1	(0.6)
Oedema Peripheral	0	(0.0)	0	(0.0)	1	(2.2)	0	(0.0)	1	(0.6)
Hepatobiliary Disorders	0	(0.0)	1	(2.2)	0	(0.0)	0	(0.0)	1	(0.6)
Cholecystitis	0	(0.0)	1	(2.2)	0	(0.0)	0	(0.0)	1	(0.6)
Infections And Infestations	2	(4.7)	4	(8.9)	3	(6.7)	1	(2.2)	10	(5.6)
Anogenital Warts	0	(0.0)	0	(0.0)	1	(2.2)	0	(0.0)	1	(0.6)
Bronchitis	0	(0.0)	1	(2.2)	0	(0.0)	0	(0.0)	1	(0.6)
Cellulitis	1	(2.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.6)

Number (%) of Patients With Specific Serious Clinical Adverse Experiences (Incidence >0% in One or More Treatment Groups) by System Organ Class - (Protocol 005: Substudies A and B Combined Entire Study Period) - *Cumulative Data*

	MK-0518 200 mg b.i.d. (N = 43)		MK-0518 400 mg b.i.d. (N = 45)		MK-0518 600 mg b.i.d. (N = 45)		Placebo (N = 45)		Total (N = 178)	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Infections And Infestations	2	(4.7)	4	(8.9)	3	(6.7)	1	(2.2)	10	(5.6)
Herpes Simplex	0	(0.0)	1	(2.2)	0	(0.0)	0	(0.0)	1	(0.6)
Leishmaniasis	0	(0.0)	0	(0.0)	1	(2.2)	0	(0.0)	1	(0.6)
Pneumonia	0	(0.0)	1	(2.2)	0	(0.0)	0	(0.0)	1	(0.6)
Sepsis	0	(0.0)	0	(0.0)	1	(2.2)	0	(0.0)	1	(0.6)
Splenic Abscess	1	(2.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.6)
Staphylococcal Abscess	1	(2.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.6)
Staphylococcal Infection	0	(0.0)	1	(2.2)	0	(0.0)	0	(0.0)	1	(0.6)
Tracheobronchitis	0	(0.0)	0	(0.0)	0	(0.0)	1	(2.2)	1	(0.6)
Injury, Poisoning And Procedural Complications	1	(2.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.6)
Laceration	1	(2.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.6)
Metabolism And Nutrition Disorders	0	(0.0)	0	(0.0)	1	(2.2)	0	(0.0)	1	(0.6)
Metabolic Acidosis	0	(0.0)	0	(0.0)	1	(2.2)	0	(0.0)	1	(0.6)
Nervous System Disorders	0	(0.0)	0	(0.0)	0	(0.0)	1	(2.2)	1	(0.6)
Facial Palsy	0	(0.0)	0	(0.0)	0	(0.0)	1	(2.2)	1	(0.6)
Headache	0	(0.0)	0	(0.0)	0	(0.0)	1	(2.2)	1	(0.6)
Lacunar Infarction	0	(0.0)	0	(0.0)	0	(0.0)	1	(2.2)	1	(0.6)
Renal And Urinary Disorders	0	(0.0)	0	(0.0)	1	(2.2)	0	(0.0)	1	(0.6)
Renal Failure	0	(0.0)	0	(0.0)	1	(2.2)	0	(0.0)	1	(0.6)
Respiratory, Thoracic And Mediastinal Disorders	1	(2.3)	1	(2.2)	0	(0.0)	0	(0.0)	2	(1.1)
Interstitial Lung Disease	0	(0.0)	1	(2.2)	0	(0.0)	0	(0.0)	1	(0.6)
Pleural Effusion	1	(2.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.6)

Number (%) of Patients With Specific Serious Clinical Adverse Experiences (Incidence >0% in One or More Treatment Groups) by System Organ Class - (Protocol 005: Substudies A and B Combined Entire Study Period) - *Cumulative Data*

	MK-0518 200 mg b.i.d. (N = 43)		MK-0518 400 mg b.i.d. (N = 45)		MK-0518 600 mg b.i.d. (N = 45)		Placebo (N = 45)		Total (N = 178)	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Skin And Subcutaneous Tissue Disorders	0	(0.0)	0	(0.0)	0	(0.0)	1	(2.2)	1	(0.6)
Lipoatrophy	0	(0.0)	0	(0.0)	0	(0.0)	1	(2.2)	1	(0.6)
Vascular Disorders	0	(0.0)	0	(0.0)	1	(2.2)	0	(0.0)	1	(0.6)
Shock	0	(0.0)	0	(0.0)	1	(2.2)	0	(0.0)	1	(0.6)

Although a patient may have had two or more clinical adverse experiences, the patient is counted only once within a category. The same patient may appear in different categories.

Note: MK-0518 and Placebo were administered with Optimized Background Therapy (OBT).

Adverse experience terms are from MedDRA Version 9.1

[Ref. 5.3.5.1: P005-Define]

Appendix 2.7.4: 44

Listing of Patients With Serious Clinical Adverse Experiences
(Protocol 005: Substudies A and B Combined Entire Study Period) - *Cumulative Data*

Study Number	AN	Gender	Race	Age	Period	Therapy	Total Daily Dose	Relative Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontinuance†	Intensity	Serious	Drug Relationship	Action Taken	Outcome
MK-0518 200 mg b.i.d.																
0050006	3286	M	white	57 yr	Post-Treatment DR	Off Drug 8 days		12	Laceration	1 day	4	severe	Y	prob not	discontinued PRx	fatal
0050007	3290	M	white	53 yr	Dose-Ranging	MK-0518	400.00 mg	260	Cellulitis	4 day	614	mod	Y	def not	no action with test drug	recovered
						MK-0518	400.00 mg	260	Staphylococcal abscess	4 day	614	mod	Y	def not	no action with test drug	recovered
0050017	3299	M	white	45 yr	Dose-Ranging	Off Drug 1 day		2	Pancreatitis acute	3 day	594	severe	Y	prob	interrupted PRx	recovered
					Open-Label Optimal	**Off Drug 1 day**		**595**	**Pancreatitis acute**	**4 day**	**594**	**severe**	**Y**	**prob not**	**interrupted PRx**	**recovered**
0050021	**3261**	**M**	**white**	**35 yr**	**Open-Label Optimal**	**MK-0518**	**800.00 mg**	**494**	**Lymphadenopathy**	**CONT**	**510**	**mod**	**Y**	**def not**	**interrupted PRx**	**fatal**
						MK-0518	**800.00 mg**	**494**	**Splenic abscess**	**CONT**	**510**	**severe**	**Y**	**def not**	**interrupted PRx**	**fatal**
						Off Drug 1 day		**511**	**Pleural effusion**	**4 day**	**510**	**severe**	**Y**	**def not**	**interrupted PRx**	**fatal**
MK-0518 400 mg b.i.d.																

Listing of Patients With Serious Clinical Adverse Experiences
(Protocol 005: Substudies A and B Combined Entire Study Period) - *Cumulative Data*

Study Number	AN	Gen-der	Race	Age	Period	Therapy	Total Daily Dose	Rela-tive Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontin-uance†	Intensity	Ser-ious	Drug Relation-ship	Action Taken	Outcome
MK-0518 400 mg b.i.d.																
0050001	3232	M	Hispa	52 yr	Dose-Ranging	MK-0518	800.00 mg	10	Irritable bowel syndrome	2 day	518	severe	Y	def not	no action with test drug	recovered
	3265	M	Hispa	35 yr	Dose-Ranging	Off Drug 1 day		78	Cholecystitis	7 day	588	severe	Y	def not	interrupted PRx	recovered
0050011	3880	M	Hispa	43 yr	Dose-Ranging	MK-0518	800.00 mg	65	Pneumonia	6 day	482	severe	Y	def not	no action with test drug	recovered
0050013	3291	M	white	42 yr	Open-Label Optimal	MK-0518	400.00 mg	367	Bronchitis	3 day	588	severe	Y	prob not	no action with test drug	recovered
0050021	3876	M	white	48 yr	Dose-Ranging	MK-0518	800.00 mg	209	Coronary artery disease	5.49 mo	375	severe	Y	prob not	no action with test drug	recovered
					Open-Label Optimal	MK-0518	800.00 mg	375	Acute myocardial infarction	7 hr	375	severe	Y	def not	discontinued PRx	fatal
0050023	3866	M	white	32 yr	Dose-Ranging	MK-0518	800.00 mg	124	Staphylococcal infection	5 day	438	severe	Y	def not	no action with test drug	recovered
0050030	2979	M	white	50 yr	Dose-Ranging	MK-0518	800.00 mg	308	Herpes simplex	8 day	586	mod	Y	def not	no action with test drug	recovered

Listing of Patients With Serious Clinical Adverse Experiences
(Protocol 005: Substudies A and B Combined Entire Study Period) - *Cumulative Data*

Study Number	AN	Gender	Race	Age	Period	Therapy	Total Daily Dose	Relative Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontinuance†	Intensity	Serious	Drug Relationship	Action Taken	Outcome
MK-0518 400 mg b.i.d.																
0050031	3274	M	white	41 yr	Dose-Ranging	MK-0518	800.00 mg	91	Interstitial lung disease	1.28 mo	346	mild	Y	def not	no action with test drug	recovered
MK-0518 600 mg b.i.d.																
0050021	3243	M	white	47 yr	Dose-Ranging	MK-0518	1200.00 mg	118	Anaemia	12 day	144	severe	Y	prob not	no action with test drug	recovered
						MK-0518	1200.00 mg	142	Metabolic acidosis	CONT	144	severe	Y	prob	interrupted PRx	not recovered
						MK-0518	1200.00 mg	142	Renal failure	CONT	144	severe	Y	prob	interrupted PRx	not recovered
						MK-0518	1200.00 mg	144	Sepsis	3 day	144	severe	Y	def not	no action with test drug	fatal
					Post-Treatment DR	Off Drug 2 days		146	Bradycardia	1 day	144	severe	Y	prob not	discontinued PRx	fatal
						Off Drug 2 days		146	Cardio-respiratory arrest	1 day	144	severe	Y	prob not	discontinued PRx	fatal

Listing of Patients With Serious Clinical Adverse Experiences
(Protocol 005: Substudies A and B Combined Entire Study Period) - *Cumulative Data*

Study Number	AN	Gen-der	Race	Age	Period	Therapy	Total Daily Dose	Rela-tive Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontin-uance†	Intensity	Ser-ious	Drug Relation-ship	Action Taken	Outcome
MK-0518 600 mg b.i.d.																
0050021	3243	M	white	47 yr	Post-Treatment DR	Off Drug 2 days		146	Shock	1 day	144	severe	Y	prob not	no action with test drug	fatal
0050027	3589	M	white	44 yr	Dose-Ranging	MK-0518	1200.00 mg	65	Oedema peripheral	3 day	455	mild	Y	def not	no action with test drug	recovered
0050030	3874	M	white	53 yr	Dose-Ranging	MK-0518	1200.00 mg	30	Anogenital warts	3 day	458	mild	Y	def not	no action with test drug	recovered
0050031	3273	M	white	45 yr	Dose-Ranging	MK-0518	1200.00 mg	8	Leishmaniasis	7 day	591	mild	Y	def not	no action with test drug	recovered
						MK-0518	1200.00 mg	101	Leishmaniasis	5 day	591	mod	Y	def not	no action with test drug	recovered
						MK-0518	1200.00 mg	122	Leishmaniasis	9 day	591	mod	Y	def not	no action with test drug	recovered
Placebo																
0050009	3272	M	black	43 yr	Dose-Ranging	Placebo	0.00 mg	61	Lacunar infarction	NA	594		Y	poss	no action with test drug	NA

Listing of Patients With Serious Clinical Adverse Experiences
(Protocol 005: Substudies A and B Combined Entire Study Period) - *Cumulative Data*

Study Number	AN	Gender	Race	Age	Period	Therapy	Total Daily Dose	Relative Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontinuance[†]	Intensity	Serious	Drug Relationship	Action Taken	Outcome
Placebo																
0050009	3272	M	black	43 yr	Open-Label Optimal	MK-0518	400.00 mg	395	Facial palsy	5 day	594	mod	Y	def not	no action with test drug	recovered
						MK-0518	400.00 mg	395	Headache	5 day	594	mod	Y	def not	no action with test drug	recovered
0050021	3225	M	white	46 yr	Dose-Ranging	Placebo	0.00 mg	121	Tracheobronchitis	7 day	469	severe	Y	def not	no action with test drug	recovered
0050022	3278	M	white	51 yr	Dose-Ranging	Placebo	0.00 mg	146	Lipoatrophy	CONT	181	severe	Y	poss	discontinued PRx	not recovered

[†]Day study therapy was discontinued relative to the start of study therapy.
Drug Relationship: def = definitely, def not = definitely not, poss = possibly, prob = probably, prob not = probably not
Intensity: mod = moderate
Note: MK-0518 and Placebo were administered with Optimized Background Therapy (OBT).
Adverse experience terms are from MedDRA Version 9.1.

[Ref. 5.3.5.1: P005-Define]

Appendix 2.7.4: 45

Listing of Patients With Serious Laboratory Adverse Experiences (Protocol 005: Substudies A and B Combined Entire Study Period) - *Cumulative Data*

Study Number	AN	Gen -der	Race	Age	Period	Therapy	Total Daily Dose	Relative Day of Onset	Adverse Experience	Relative Day of Discontin -uance†	Serious	Drug Relation-ship	Action Taken
MK-0518 600 mg b.i.d.													
0050003	**3294**	**M**	**Asian**	**35 yr**	**Open-Label Optimal**	**MK-0518**	**400.00 mg**	**606**	**Platelet count decreased**	**606**	**Y**	**poss**	**no action with test drug**

†Day study therapy was discontinued relative to the start of study therapy.
Drug Relationship: def = definitely, def not = definitely not, poss = possibly, prob = probably, prob not = probably not
Note: MK-0518 and Placebo were administered with Optimized Background Therapy (OBT).
Adverse experience terms are from MedDRA Version 9.1.

[Ref. 5.3.5.1: P005-Define]

Appendix 2.7.4: 46

Number (%) of Patients With Specific Serious Clinical Adverse Experiences (Incidence >0% in One or More Treatment Groups) by System Organ Class - Treatment-Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Cumulative Data*

	MK-0518 400 mg b.i.d. (N = 507)		Placebo (N = 282)		Total (N = 789)	
	n	(%)	n	(%)	n	(%)
Patients With One Or More Adverse Experiences	68	(13.4)	40	(14.2)	108	(13.7)
Patients With No Adverse Experience	439	(86.6)	242	(85.8)	681	(86.3)
Blood And Lymphatic System Disorders	3	(0.6)	3	(1.1)	6	(0.8)
Anaemia	2	(0.4)	0	(0.0)	2	(0.3)
Haemolytic Anaemia	1	(0.2)	0	(0.0)	1	(0.1)
Leukopenia	0	(0.0)	1	(0.4)	1	(0.1)
Neutropenia	1	(0.2)	2	(0.7)	3	(0.4)
Cardiac Disorders	6	(1.2)	3	(1.1)	9	(1.1)
Angina Pectoris	1	(0.2)	0	(0.0)	1	(0.1)
Cardiac Failure Congestive	1	(0.2)	0	(0.0)	1	(0.1)
Coronary Artery Disease	2	(0.4)	1	(0.4)	3	(0.4)
Mitral Valve Incompetence	0	(0.0)	1	(0.4)	1	(0.1)
Myocardial Infarction	2	(0.4)	1	(0.4)	3	(0.4)
Pericarditis	1	(0.2)	0	(0.0)	1	(0.1)
Ear And Labyrinth Disorders	0	(0.0)	2	(0.7)	2	(0.3)
Hypoacusis	0	(0.0)	1	(0.4)	1	(0.1)
Vertigo	0	(0.0)	1	(0.4)	1	(0.1)
Endocrine Disorders	1	(0.2)	0	(0.0)	1	(0.1)
Hyperthyroidism	1	(0.2)	0	(0.0)	1	(0.1)
Eye Disorders	1	(0.2)	1	(0.4)	2	(0.3)
Endophthalmitis	1	(0.2)	0	(0.0)	1	(0.1)

Number (%) of Patients With Specific Serious Clinical Adverse Experiences (Incidence >0% in One or More Treatment Groups) by System Organ Class - Treatment-Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Cumulative Data*

	MK-0518 400 mg b.i.d. (N = 507)		Placebo (N = 282)		Total (N = 789)	
	n	(%)	n	(%)	n	(%)
Eye Disorders	1	(0.2)	1	(0.4)	2	(0.3)
Uveitis	0	(0.0)	1	(0.4)	1	(0.1)
Gastrointestinal Disorders	9	(1.8)	3	(1.1)	12	(1.5)
Abdominal Pain	2	(0.4)	0	(0.0)	2	(0.3)
Anal Fistula	0	(0.0)	1	(0.4)	1	(0.1)
Diarrhoea	1	(0.2)	0	(0.0)	1	(0.1)
Gastritis	1	(0.2)	0	(0.0)	1	(0.1)
Haemorrhoids	0	(0.0)	1	(0.4)	1	(0.1)
Irritable Bowel Syndrome	1	(0.2)	0	(0.0)	1	(0.1)
Nausea	1	(0.2)	0	(0.0)	1	(0.1)
Pancreatitis	0	(0.0)	1	(0.4)	1	(0.1)
Rectal Haemorrhage	1	(0.2)	0	(0.0)	1	(0.1)
Rectal Stenosis	0	(0.0)	1	(0.4)	1	(0.1)
Small Intestinal Obstruction	1	(0.2)	0	(0.0)	1	(0.1)
Upper Gastrointestinal Haemorrhage	1	(0.2)	0	(0.0)	1	(0.1)
Varices Oesophageal	1	(0.2)	0	(0.0)	1	(0.1)
Vomiting	1	(0.2)	0	(0.0)	1	(0.1)
General Disorders And Administration Site Conditions	7	(1.4)	5	(1.8)	12	(1.5)
Asthenia	0	(0.0)	2	(0.7)	2	(0.3)
Chest Pain	1	(0.2)	0	(0.0)	1	(0.1)
Malaise	2	(0.4)	0	(0.0)	2	(0.3)
Mass	1	(0.2)	0	(0.0)	1	(0.1)

Number (%) of Patients With Specific Serious Clinical Adverse Experiences (Incidence >0% in One or More Treatment Groups) by System Organ Class - Treatment-Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Cumulative Data*

	MK-0518 400 mg b.i.d. (N = 507)		Placebo (N = 282)		Total (N = 789)	
	n	(%)	n	(%)	n	(%)
General Disorders And Administration Site Conditions	7	(1.4)	5	(1.8)	12	(1.5)
Multi-Organ Failure	1	(0.2)	0	(0.0)	1	(0.1)
Oedema Peripheral	1	(0.2)	0	(0.0)	1	(0.1)
Pyrexia	2	(0.4)	4	(1.4)	6	(0.8)
Hepatobiliary Disorders	4	(0.8)	2	(0.7)	6	(0.8)
Cholangitis	1	(0.2)	0	(0.0)	1	(0.1)
Cholecystitis	1	(0.2)	0	(0.0)	1	(0.1)
Gallbladder Disorder	0	(0.0)	1	(0.4)	1	(0.1)
Hepatitis	1	(0.2)	0	(0.0)	1	(0.1)
Hepatitis Toxic	0	(0.0)	1	(0.4)	1	(0.1)
Portal Hypertension	1	(0.2)	0	(0.0)	1	(0.1)
Immune System Disorders	4	(0.8)	0	(0.0)	4	(0.5)
Drug Hypersensitivity	1	(0.2)	0	(0.0)	1	(0.1)
Hypersensitivity	2	(0.4)	0	(0.0)	2	(0.3)
Immune Reconstitution Syndrome	2	(0.4)	0	(0.0)	2	(0.3)
Infections And Infestations	29	(5.7)	15	(5.3)	44	(5.6)
AIDS Dementia Complex	0	(0.0)	1	(0.4)	1	(0.1)
Abscess Bacterial	1	(0.2)	0	(0.0)	1	(0.1)
Acinetobacter Bacteraemia	1	(0.2)	0	(0.0)	1	(0.1)
Appendicitis	1	(0.2)	0	(0.0)	1	(0.1)
Aspergillosis	1	(0.2)	0	(0.0)	1	(0.1)
Atypical Mycobacterial Lymphadenitis	0	(0.0)	1	(0.4)	1	(0.1)

Number (%) of Patients With Specific Serious Clinical Adverse Experiences (Incidence >0% in One or More Treatment Groups) by System Organ Class - Treatment-Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Cumulative Data*

	MK-0518 400 mg b.i.d. (N = 507)		Placebo (N = 282)		Total (N = 789)	
	n	(%)	n	(%)	n	(%)
Infections And Infestations	29	(5.7)	15	(5.3)	44	(5.6)
Bronchopneumonia	1	(0.2)	0	(0.0)	1	(0.1)
Cellulitis	2	(0.4)	0	(0.0)	2	(0.3)
Choriomeningitis Lymphocytic	2	(0.4)	0	(0.0)	2	(0.3)
Cytomegalovirus Chorioretinitis	0	(0.0)	2	(0.7)	2	(0.3)
Cytomegalovirus Colitis	1	(0.2)	1	(0.4)	2	(0.3)
Cytomegalovirus Infection	1	(0.2)	0	(0.0)	1	(0.1)
Endocarditis	0	(0.0)	1	(0.4)	1	(0.1)
Erythema Infectiosum	0	(0.0)	1	(0.4)	1	(0.1)
Gastroenteritis	0	(0.0)	1	(0.4)	1	(0.1)
Gastroenteritis Cryptosporidial	0	(0.0)	1	(0.4)	1	(0.1)
Gastroenteritis Salmonella	0	(0.0)	1	(0.4)	1	(0.1)
HIV Infection	1	(0.2)	0	(0.0)	1	(0.1)
Herpes Simplex	2	(0.4)	0	(0.0)	2	(0.3)
Infection	1	(0.2)	0	(0.0)	1	(0.1)
Meningitis Cryptococcal	2	(0.4)	0	(0.0)	2	(0.3)
Mycobacterial Infection	1	(0.2)	0	(0.0)	1	(0.1)
Oesophageal Candidiasis	1	(0.2)	3	(1.1)	4	(0.5)
Oral Candidiasis	0	(0.0)	1	(0.4)	1	(0.1)
Otitis Media	1	(0.2)	0	(0.0)	1	(0.1)
Pneumonia	7	(1.4)	4	(1.4)	11	(1.4)
Pneumonia Pneumococcal	1	(0.2)	0	(0.0)	1	(0.1)

Number (%) of Patients With Specific Serious Clinical Adverse Experiences (Incidence >0% in One or More Treatment Groups) by System Organ Class - Treatment-Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Cumulative Data*

	MK-0518 400 mg b.i.d. (N = 507)		Placebo (N = 282)		Total (N = 789)	
	n	(%)	n	(%)	n	(%)
Infections And Infestations	29	(5.7)	15	(5.3)	44	(5.6)
Pseudomonal Sepsis	0	(0.0)	1	(0.4)	1	(0.1)
Retroviral Infection	1	(0.2)	0	(0.0)	1	(0.1)
Salmonella Bacteraemia	0	(0.0)	1	(0.4)	1	(0.1)
Septic Shock	2	(0.4)	1	(0.4)	3	(0.4)
Sinusitis	1	(0.2)	0	(0.0)	1	(0.1)
Staphylococcal Infection	1	(0.2)	0	(0.0)	1	(0.1)
Subcutaneous Abscess	1	(0.2)	0	(0.0)	1	(0.1)
Tracheobronchitis	0	(0.0)	1	(0.4)	1	(0.1)
Tuberculosis	1	(0.2)	0	(0.0)	1	(0.1)
Viral Infection	1	(0.2)	0	(0.0)	1	(0.1)
Injury, Poisoning And Procedural Complications	8	(1.6)	3	(1.1)	11	(1.4)
Accidental Overdose	1	(0.2)	0	(0.0)	1	(0.1)
Hip Fracture	0	(0.0)	1	(0.4)	1	(0.1)
Humerus Fracture	1	(0.2)	0	(0.0)	1	(0.1)
Incisional Hernia	1	(0.2)	0	(0.0)	1	(0.1)
Intentional Overdose	1	(0.2)	1	(0.4)	2	(0.3)
Lower Limb Fracture	1	(0.2)	0	(0.0)	1	(0.1)
Overdose	1	(0.2)	0	(0.0)	1	(0.1)
Post Procedural Haemorrhage	1	(0.2)	0	(0.0)	1	(0.1)
Spinal Fracture	1	(0.2)	0	(0.0)	1	(0.1)
Thoracic Vertebral Fracture	0	(0.0)	1	(0.4)	1	(0.1)

Number (%) of Patients With Specific Serious Clinical Adverse Experiences (Incidence >0% in One or More Treatment Groups) by System Organ Class - Treatment-Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Cumulative Data*

	MK-0518 400 mg b.i.d. (N = 507)		Placebo (N = 282)		Total (N = 789)	
	n	(%)	n	(%)	n	(%)
Investigations	1	(0.2)	0	(0.0)	1	(0.1)
Weight Decreased	1	(0.2)	0	(0.0)	1	(0.1)
Metabolism And Nutrition Disorders	3	(0.6)	2	(0.7)	5	(0.6)
Dehydration	3	(0.6)	0	(0.0)	3	(0.4)
Hyperglycaemia	0	(0.0)	1	(0.4)	1	(0.1)
Malnutrition	0	(0.0)	1	(0.4)	1	(0.1)
Musculoskeletal And Connective Tissue Disorders	1	(0.2)	2	(0.7)	3	(0.4)
Bone Pain	1	(0.2)	0	(0.0)	1	(0.1)
Intervertebral Disc Protrusion	0	(0.0)	1	(0.4)	1	(0.1)
Osteoporotic Fracture	0	(0.0)	1	(0.4)	1	(0.1)
Neoplasms Benign, Malignant And Unspecified (Incl Cysts And Polyps)	11	(2.2)	0	(0.0)	11	(1.4)
B-Cell Lymphoma	1	(0.2)	0	(0.0)	1	(0.1)
Hepatic Neoplasm Malignant	1	(0.2)	0	(0.0)	1	(0.1)
Kaposi's Sarcoma AIDS Related	2	(0.4)	0	(0.0)	2	(0.3)
Lymphoma	1	(0.2)	0	(0.0)	1	(0.1)
Metastatic Squamous Cell Carcinoma	1	(0.2)	0	(0.0)	1	(0.1)
Rectal Cancer	1	(0.2)	0	(0.0)	1	(0.1)
Rectal Cancer Stage 0	1	(0.2)	0	(0.0)	1	(0.1)
Squamous Cell Carcinoma	2	(0.4)	0	(0.0)	2	(0.3)
T-Cell Lymphoma	1	(0.2)	0	(0.0)	1	(0.1)
Nervous System Disorders	6	(1.2)	5	(1.8)	11	(1.4)
Convulsion	1	(0.2)	1	(0.4)	2	(0.3)

Number (%) of Patients With Specific Serious Clinical Adverse Experiences (Incidence >0% in One or More Treatment Groups) by System Organ Class - Treatment-Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Cumulative Data*

	MK-0518 400 mg b.i.d. (N = 507)		Placebo (N = 282)		Total (N = 789)	
	n	(%)	n	(%)	n	(%)
Nervous System Disorders	6	(1.2)	5	(1.8)	11	(1.4)
Encephalitis	1	(0.2)	0	(0.0)	1	(0.1)
Epilepsy	0	(0.0)	1	(0.4)	1	(0.1)
Lacunar Infarction	0	(0.0)	1	(0.4)	1	(0.1)
Migraine	1	(0.2)	1	(0.4)	2	(0.3)
Neuralgia	1	(0.2)	0	(0.0)	1	(0.1)
Poor Quality Sleep	0	(0.0)	1	(0.4)	1	(0.1)
Presyncope	1	(0.2)	0	(0.0)	1	(0.1)
Psychomotor Hyperactivity	0	(0.0)	1	(0.4)	1	(0.1)
Syncope	1	(0.2)	0	(0.0)	1	(0.1)
Psychiatric Disorders	3	(0.6)	2	(0.7)	5	(0.6)
Depression	2	(0.4)	1	(0.4)	3	(0.4)
Mental Status Changes	1	(0.2)	0	(0.0)	1	(0.1)
Panic Attack	0	(0.0)	1	(0.4)	1	(0.1)
Renal And Urinary Disorders	4	(0.8)	3	(1.1)	7	(0.9)
Focal Glomerulosclerosis	1	(0.2)	0	(0.0)	1	(0.1)
Nephrolithiasis	0	(0.0)	1	(0.4)	1	(0.1)
Nephropathy	0	(0.0)	1	(0.4)	1	(0.1)
Nephropathy Toxic	1	(0.2)	0	(0.0)	1	(0.1)
Nephrotic Syndrome	1	(0.2)	0	(0.0)	1	(0.1)
Renal Failure	1	(0.2)	1	(0.4)	2	(0.3)
Renal Failure Chronic	1	(0.2)	0	(0.0)	1	(0.1)

Number (%) of Patients With Specific Serious Clinical Adverse Experiences (Incidence >0% in One or More Treatment Groups) by System Organ Class - Treatment-Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Cumulative Data*

	MK-0518 400 mg b.i.d. (N = 507)		Placebo (N = 282)		Total (N = 789)	
	n	(%)	n	(%)	n	(%)
Renal And Urinary Disorders	4	(0.8)	3	(1.1)	7	(0.9)
Renal Tubular Necrosis	1	(0.2)	0	(0.0)	1	(0.1)
Reproductive System And Breast Disorders	2	(0.4)	2	(0.7)	4	(0.5)
Benign Prostatic Hyperplasia	1	(0.2)	0	(0.0)	1	(0.1)
Gynaecomastia	0	(0.0)	1	(0.4)	1	(0.1)
Oedema Genital	0	(0.0)	1	(0.4)	1	(0.1)
Prostatitis	1	(0.2)	0	(0.0)	1	(0.1)
Respiratory, Thoracic And Mediastinal Disorders	3	(0.6)	1	(0.4)	4	(0.5)
Asthma	2	(0.4)	0	(0.0)	2	(0.3)
Interstitial Lung Disease	1	(0.2)	0	(0.0)	1	(0.1)
Pulmonary Hypertension	0	(0.0)	1	(0.4)	1	(0.1)
Skin And Subcutaneous Tissue Disorders	0	(0.0)	1	(0.4)	1	(0.1)
Lipoatrophy	0	(0.0)	1	(0.4)	1	(0.1)
Vascular Disorders	2	(0.4)	3	(1.1)	5	(0.6)
Deep Vein Thrombosis	1	(0.2)	0	(0.0)	1	(0.1)
Hypotension	0	(0.0)	1	(0.4)	1	(0.1)
Infarction	0	(0.0)	1	(0.4)	1	(0.1)
Shock	1	(0.2)	0	(0.0)	1	(0.1)
Varicophlebitis	0	(0.0)	1	(0.4)	1	(0.1)

Although a patient may have had two or more serious clinical adverse experiences, the patient is counted only once within a category. The same patient may appear in different categories.

Note: MK-0518 and Placebo were administered with Optimized Background Therapy (OBT).

Adverse experience terms are from MedDRA Version 9.1.

[Ref. 5.3.5.1: P005-Define, P018-Define, P019-Define]

Appendix 2.7.4: 47

Number (%) of Patients With Specific Serious Clinical Adverse Experiences (Incidence >0% in One or More Treatment Groups) by System Organ Class - Treatment-Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Original Application*

	MK-0518 400 mg b.i.d. (N = 507)		Placebo (N = 282)		Total (N = 789)	
	n	(%)	n	(%)	n	(%)
Patients With One Or More Serious Adverse Experiences	54	(10.7)	36	(12.8)	90	(11.4)
Patients With No Serious Adverse Experience	453	(89.3)	246	(87.2)	699	(88.6)
Blood And Lymphatic System Disorders	2	(0.4)	3	(1.1)	5	(0.6)
Anaemia	2	(0.4)	0	(0.0)	2	(0.3)
Leukopenia	0	(0.0)	1	(0.4)	1	(0.1)
Neutropenia	1	(0.2)	2	(0.7)	3	(0.4)
Cardiac Disorders	4	(0.8)	3	(1.1)	7	(0.9)
Cardiac Failure Congestive	1	(0.2)	0	(0.0)	1	(0.1)
Coronary Artery Disease	1	(0.2)	1	(0.4)	2	(0.3)
Mitral Valve Incompetence	0	(0.0)	1	(0.4)	1	(0.1)
Myocardial Infarction	1	(0.2)	1	(0.4)	2	(0.3)
Pericarditis	1	(0.2)	0	(0.0)	1	(0.1)
Congenital, Familial And Genetic Disorders	0	(0.0)	1	(0.4)	1	(0.1)
Preternatural Anus	0	(0.0)	1	(0.4)	1	(0.1)
Ear And Labyrinth Disorders	0	(0.0)	2	(0.7)	2	(0.3)
Hypoacusis	0	(0.0)	1	(0.4)	1	(0.1)
Vertigo	0	(0.0)	1	(0.4)	1	(0.1)
Endocrine Disorders	1	(0.2)	0	(0.0)	1	(0.1)
Hyperthyroidism	1	(0.2)	0	(0.0)	1	(0.1)
Eye Disorders	1	(0.2)	1	(0.4)	2	(0.3)
Endophthalmitis	1	(0.2)	0	(0.0)	1	(0.1)
Uveitis	0	(0.0)	1	(0.4)	1	(0.1)

Number (%) of Patients With Specific Serious Clinical Adverse Experiences (Incidence >0% in One or More Treatment Groups) by System Organ Class - Treatment-Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Original Application*

	MK-0518 400 mg b.i.d. (N = 507)		Placebo (N = 282)		Total (N = 789)	
	n	(%)	n	(%)	n	(%)
Gastrointestinal Disorders	6	(1.2)	4	(1.4)	10	(1.3)
Abdominal Pain	1	(0.2)	0	(0.0)	1	(0.1)
Anal Fistula	0	(0.0)	1	(0.4)	1	(0.1)
Diarrhoea	0	(0.0)	1	(0.4)	1	(0.1)
Gastritis	1	(0.2)	0	(0.0)	1	(0.1)
Haemorrhoids	0	(0.0)	1	(0.4)	1	(0.1)
Irritable Bowel Syndrome	1	(0.2)	0	(0.0)	1	(0.1)
Nausea	1	(0.2)	0	(0.0)	1	(0.1)
Pancreatitis	0	(0.0)	1	(0.4)	1	(0.1)
Rectal Haemorrhage	1	(0.2)	0	(0.0)	1	(0.1)
Rectal Stenosis	0	(0.0)	1	(0.4)	1	(0.1)
Small Intestinal Obstruction	1	(0.2)	0	(0.0)	1	(0.1)
Upper Gastrointestinal Haemorrhage	1	(0.2)	0	(0.0)	1	(0.1)
Vomiting	1	(0.2)	0	(0.0)	1	(0.1)
General Disorders And Administration Site Conditions	5	(1.0)	4	(1.4)	9	(1.1)
Asthenia	0	(0.0)	2	(0.7)	2	(0.3)
Malaise	2	(0.4)	0	(0.0)	2	(0.3)
Multi-Organ Failure	1	(0.2)	0	(0.0)	1	(0.1)
Oedema Peripheral	1	(0.2)	0	(0.0)	1	(0.1)
Pyrexia	2	(0.4)	3	(1.1)	5	(0.6)
Hepatobiliary Disorders	3	(0.6)	1	(0.4)	4	(0.5)
Cholangitis	1	(0.2)	0	(0.0)	1	(0.1)
Cholecystitis	1	(0.2)	0	(0.0)	1	(0.1)

Number (%) of Patients With Specific Serious Clinical Adverse Experiences (Incidence >0% in One or More Treatment Groups) by System Organ Class - Treatment-Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Original Application*

	MK-0518 400 mg b.i.d. (N = 507)		Placebo (N = 282)		Total (N = 789)	
	n	(%)	n	(%)	n	(%)
Hepatobiliary Disorders	3	(0.6)	1	(0.4)	4	(0.5)
Gallbladder Disorder	0	(0.0)	1	(0.4)	1	(0.1)
Hepatitis	1	(0.2)	0	(0.0)	1	(0.1)
Immune System Disorders	4	(0.8)	0	(0.0)	4	(0.5)
Drug Hypersensitivity	1	(0.2)	0	(0.0)	1	(0.1)
Hypersensitivity	2	(0.4)	0	(0.0)	2	(0.3)
Immune Reconstitution Syndrome	2	(0.4)	0	(0.0)	2	(0.3)
Infections And Infestations	25	(4.9)	12	(4.3)	37	(4.7)
AIDS Dementia Complex	0	(0.0)	1	(0.4)	1	(0.1)
Abscess Bacterial	1	(0.2)	0	(0.0)	1	(0.1)
Acinetobacter Bacteraemia	1	(0.2)	0	(0.0)	1	(0.1)
Acute HIV Infection	1	(0.2)	0	(0.0)	1	(0.1)
Bronchopneumonia	1	(0.2)	0	(0.0)	1	(0.1)
Bronchopulmonary Aspergillosis	1	(0.2)	0	(0.0)	1	(0.1)
Cellulitis	2	(0.4)	0	(0.0)	2	(0.3)
Cytomegalovirus Chorioretinitis	0	(0.0)	2	(0.7)	2	(0.3)
Cytomegalovirus Colitis	1	(0.2)	1	(0.4)	2	(0.3)
Cytomegalovirus Infection	1	(0.2)	0	(0.0)	1	(0.1)
Erythema Infectiosum	0	(0.0)	1	(0.4)	1	(0.1)
Gastroenteritis Cryptosporidial	0	(0.0)	1	(0.4)	1	(0.1)
Gastroenteritis Salmonella	0	(0.0)	1	(0.4)	1	(0.1)
Herpes Simplex	1	(0.2)	0	(0.0)	1	(0.1)
Infection	1	(0.2)	0	(0.0)	1	(0.1)

Number (%) of Patients With Specific Serious Clinical Adverse Experiences (Incidence >0% in One or More Treatment Groups) by System Organ Class - Treatment-Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Original Application*

	MK-0518 400 mg b.i.d. (N = 507)		Placebo (N = 282)		Total (N = 789)	
	n	(%)	n	(%)	n	(%)
Infections And Infestations	25	(4.9)	12	(4.3)	37	(4.7)
Meningitis	2	(0.4)	0	(0.0)	2	(0.3)
Meningitis Cryptococcal	2	(0.4)	0	(0.0)	2	(0.3)
Mycobacterial Infection	1	(0.2)	0	(0.0)	1	(0.1)
Mycobacterium Avium Complex Infection	0	(0.0)	1	(0.4)	1	(0.1)
Oesophageal Candidiasis	1	(0.2)	3	(1.1)	4	(0.5)
Oral Candidiasis	0	(0.0)	1	(0.4)	1	(0.1)
Otitis Media	1	(0.2)	0	(0.0)	1	(0.1)
Pneumonia	6	(1.2)	3	(1.1)	9	(1.1)
Pneumonia Pneumococcal	1	(0.2)	0	(0.0)	1	(0.1)
Pseudomonal Sepsis	0	(0.0)	1	(0.4)	1	(0.1)
Pulmonary Tuberculosis	1	(0.2)	0	(0.0)	1	(0.1)
Salmonella Bacteraemia	0	(0.0)	1	(0.4)	1	(0.1)
Septic Shock	2	(0.4)	1	(0.4)	3	(0.4)
Sinusitis	1	(0.2)	0	(0.0)	1	(0.1)
Staphylococcal Infection	1	(0.2)	0	(0.0)	1	(0.1)
Subcutaneous Abscess	1	(0.2)	0	(0.0)	1	(0.1)
Tracheobronchitis	0	(0.0)	1	(0.4)	1	(0.1)
Viral Infection	1	(0.2)	0	(0.0)	1	(0.1)
Injury, Poisoning And Procedural Complications	7	(1.4)	2	(0.7)	9	(1.1)
Hip Fracture	0	(0.0)	1	(0.4)	1	(0.1)
Humerus Fracture	1	(0.2)	0	(0.0)	1	(0.1)
Incisional Hernia	1	(0.2)	0	(0.0)	1	(0.1)

Number (%) of Patients With Specific Serious Clinical Adverse Experiences (Incidence >0% in One or More Treatment Groups) by System Organ Class - Treatment-Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Original Application*

	MK-0518 400 mg b.i.d. (N = 507)		Placebo (N = 282)		Total (N = 789)	
	n	(%)	n	(%)	n	(%)
Injury, Poisoning And Procedural Complications	7	(1.4)	2	(0.7)	9	(1.1)
Intentional Overdose	1	(0.2)	0	(0.0)	1	(0.1)
Lower Limb Fracture	1	(0.2)	0	(0.0)	1	(0.1)
Overdose	1	(0.2)	0	(0.0)	1	(0.1)
Post Procedural Haemorrhage	1	(0.2)	0	(0.0)	1	(0.1)
Spinal Fracture	1	(0.2)	0	(0.0)	1	(0.1)
Thoracic Vertebral Fracture	0	(0.0)	1	(0.4)	1	(0.1)
Investigations	1	(0.2)	0	(0.0)	1	(0.1)
Weight Decreased	1	(0.2)	0	(0.0)	1	(0.1)
Metabolism And Nutrition Disorders	3	(0.6)	1	(0.4)	4	(0.5)
Dehydration	3	(0.6)	0	(0.0)	3	(0.4)
Hyperglycaemia	0	(0.0)	1	(0.4)	1	(0.1)
Musculoskeletal And Connective Tissue Disorders	1	(0.2)	2	(0.7)	3	(0.4)
Bone Pain	1	(0.2)	0	(0.0)	1	(0.1)
Intervertebral Disc Protrusion	0	(0.0)	1	(0.4)	1	(0.1)
Osteoporotic Fracture	0	(0.0)	1	(0.4)	1	(0.1)
Neoplasms Benign, Malignant And Unspecified (Incl Cysts And Polyps)	10	(2.0)	0	(0.0)	10	(1.3)
Anal Cancer Stage 0	1	(0.2)	0	(0.0)	1	(0.1)
B-Cell Lymphoma	1	(0.2)	0	(0.0)	1	(0.1)
Hepatic Neoplasm Malignant	1	(0.2)	0	(0.0)	1	(0.1)
Kaposi's Sarcoma	2	(0.4)	0	(0.0)	2	(0.3)
Lymphoma	2	(0.4)	0	(0.0)	2	(0.3)
Rectal Cancer	1	(0.2)	0	(0.0)	1	(0.1)

Number (%) of Patients With Specific Serious Clinical Adverse Experiences (Incidence >0% in One or More Treatment Groups) by System Organ Class - Treatment-Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Original Application*

	MK-0518 400 mg b.i.d. (N = 507)		Placebo (N = 282)		Total (N = 789)	
	n	(%)	n	(%)	n	(%)
Neoplasms Benign, Malignant And Unspecified (Incl Cysts And Polyps)	10	(2.0)	0	(0.0)	10	(1.3)
Squamous Cell Carcinoma	2	(0.4)	0	(0.0)	2	(0.3)
Nervous System Disorders	4	(0.8)	4	(1.4)	8	(1.0)
Convulsion	0	(0.0)	1	(0.4)	1	(0.1)
Encephalitis	1	(0.2)	0	(0.0)	1	(0.1)
Epilepsy	0	(0.0)	1	(0.4)	1	(0.1)
Lacunar Infarction	0	(0.0)	1	(0.4)	1	(0.1)
Migraine	0	(0.0)	1	(0.4)	1	(0.1)
Neuralgia	1	(0.2)	0	(0.0)	1	(0.1)
Presyncope	1	(0.2)	0	(0.0)	1	(0.1)
Psychomotor Hyperactivity	0	(0.0)	1	(0.4)	1	(0.1)
Syncope	1	(0.2)	0	(0.0)	1	(0.1)
Psychiatric Disorders	3	(0.6)	1	(0.4)	4	(0.5)
Depression	2	(0.4)	1	(0.4)	3	(0.4)
Mental Status Changes	1	(0.2)	0	(0.0)	1	(0.1)
Renal And Urinary Disorders	3	(0.6)	2	(0.7)	5	(0.6)
Nephrolithiasis	0	(0.0)	1	(0.4)	1	(0.1)
Nephropathy	0	(0.0)	1	(0.4)	1	(0.1)
Nephropathy Toxic	1	(0.2)	0	(0.0)	1	(0.1)
Renal Failure	2	(0.4)	0	(0.0)	2	(0.3)
Renal Tubular Necrosis	1	(0.2)	0	(0.0)	1	(0.1)
Reproductive System And Breast Disorders	2	(0.4)	0	(0.0)	2	(0.3)
Benign Prostatic Hyperplasia	1	(0.2)	0	(0.0)	1	(0.1)

Number (%) of Patients With Specific Serious Clinical Adverse Experiences (Incidence >0% in One or More Treatment Groups) by System Organ Class - Treatment-Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Original Application*

	MK-0518 400 mg b.i.d. (N = 507)		Placebo (N = 282)		Total (N = 789)	
	n	(%)	n	(%)	n	(%)
Reproductive System And Breast Disorders	2	(0.4)	0	(0.0)	2	(0.3)
Prostatitis	1	(0.2)	0	(0.0)	1	(0.1)
Respiratory, Thoracic And Mediastinal Disorders	3	(0.6)	1	(0.4)	4	(0.5)
Asthma	2	(0.4)	0	(0.0)	2	(0.3)
Interstitial Lung Disease	1	(0.2)	0	(0.0)	1	(0.1)
Pulmonary Hypertension	0	(0.0)	1	(0.4)	1	(0.1)
Skin And Subcutaneous Tissue Disorders	0	(0.0)	1	(0.4)	1	(0.1)
Lipoatrophy	0	(0.0)	1	(0.4)	1	(0.1)
Vascular Disorders	2	(0.4)	2	(0.7)	4	(0.5)
Deep Vein Thrombosis	1	(0.2)	0	(0.0)	1	(0.1)
Hypotension	0	(0.0)	1	(0.4)	1	(0.1)
Shock	1	(0.2)	0	(0.0)	1	(0.1)
Varicophlebitis	0	(0.0)	1	(0.4)	1	(0.1)

Although a patient may have had two or more serious clinical adverse experiences, the patient is counted only once within a category. The same patient may appear in different categories.

Note: MK-0518 and Placebo were administered with Optimized Background Therapy (OBT).

Adverse experience terms are from MedDRA Version 9.1.

[Ref. 5.3.5.1: P005, P018, P019]

Appendix 2.7.4: 48

Number (%) of Patients With Specific Serious and Drug-Related (Overall) Clinical Adverse Experiences (Incidence >0% in One or More Treatment Groups) by System Organ Class—Treatment-Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019)
- Cumulative Data

	MK-0518 400 mg b.i.d. (N = 507)		Placebo (N = 282)		Total (N = 789)	
	n	(%)	n	(%)	n	(%)
Patients With One Or More Adverse Experiences	11	(2.2)	7	(2.5)	18	(2.3)
Patients With No Adverse Experience	496	(97.8)	275	(97.5)	771	(97.7)
Blood And Lymphatic System Disorders	1	(0.2)	1	(0.4)	2	(0.3)
Anaemia	1	(0.2)	0	(0.0)	1	(0.1)
Neutropenia	1	(0.2)	1	(0.4)	2	(0.3)
Cardiac Disorders	1	(0.2)	0	(0.0)	1	(0.1)
Myocardial Infarction	1	(0.2)	0	(0.0)	1	(0.1)
Gastrointestinal Disorders	1	(0.2)	1	(0.4)	2	(0.3)
Gastritis	1	(0.2)	0	(0.0)	1	(0.1)
Pancreatitis	0	(0.0)	1	(0.4)	1	(0.1)
Hepatobiliary Disorders	1	(0.2)	1	(0.4)	2	(0.3)
Hepatitis	1	(0.2)	0	(0.0)	1	(0.1)
Hepatitis Toxic	0	(0.0)	1	(0.4)	1	(0.1)
Immune System Disorders	2	(0.4)	0	(0.0)	2	(0.3)
Drug Hypersensitivity	1	(0.2)	0	(0.0)	1	(0.1)
Hypersensitivity	2	(0.4)	0	(0.0)	2	(0.3)
Infections And Infestations	1	(0.2)	0	(0.0)	1	(0.1)
Herpes Simplex	1	(0.2)	0	(0.0)	1	(0.1)
Injury, Poisoning And Procedural Complications	1	(0.2)	0	(0.0)	1	(0.1)
Accidental Overdose	1	(0.2)	0	(0.0)	1	(0.1)
Metabolism And Nutrition Disorders	0	(0.0)	1	(0.4)	1	(0.1)

Number (%) of Patients With Specific Serious and Drug-Related (Overall) Clinical Adverse Experiences (Incidence >0% in One or More Treatment Groups) by System Organ Class—Treatment-Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019)
- Cumulative Data

	MK-0518 400 mg b.i.d. (N = 507)		Placebo (N = 282)		Total (N = 789)	
	n	(%)	n	(%)	n	(%)
Metabolism And Nutrition Disorders	0	(0.0)	1	(0.4)	1	(0.1)
Hyperglycaemia	0	(0.0)	1	(0.4)	1	(0.1)
Nervous System Disorders	0	(0.0)	1	(0.4)	1	(0.1)
Lacunar Infarction	0	(0.0)	1	(0.4)	1	(0.1)
Renal And Urinary Disorders	3	(0.6)	2	(0.7)	5	(0.6)
Nephrolithiasis	0	(0.0)	1	(0.4)	1	(0.1)
Nephropathy Toxic	1	(0.2)	0	(0.0)	1	(0.1)
Renal Failure	1	(0.2)	1	(0.4)	2	(0.3)
Renal Failure Chronic	1	(0.2)	0	(0.0)	1	(0.1)
Renal Tubular Necrosis	1	(0.2)	0	(0.0)	1	(0.1)
Skin And Subcutaneous Tissue Disorders	0	(0.0)	1	(0.4)	1	(0.1)
Lipoatrophy	0	(0.0)	1	(0.4)	1	(0.1)

Although a patient may have had two or more serious and drug-related clinical adverse experiences, the patient is counted only once within a category. The same patient may appear in different categories.

Note: MK-0518 and Placebo were administered with Optimized Background Therapy (OBT).

Adverse experience terms are from MedDRA Version 9.1

[Ref. 5.3.5.1: P005-Define, P018-Define, P019-Define]

Appendix 2.7.4: 49

Number (%) of Patients With Specific Serious and Drug-Related (Overall) Clinical Adverse Experiences (Incidence >0% in One or More Treatment Groups) by System Organ Class—Treatment-Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019)
- Original Application

	MK-0518 400 mg b.i.d. (N = 507)		Placebo (N = 282)		Total (N = 789)	
	n	(%)	n	(%)	n	(%)
Patients With One Or More Serious and Drug-Related Adverse Experiences	8	(1.6)	5	(1.8)	13	(1.6)
Patients With No Serious and Drug-Related Adverse Experience	499	(98.4)	277	(98.2)	776	(98.4)
Blood And Lymphatic System Disorders	1	(0.2)	1	(0.4)	2	(0.3)
Anaemia	1	(0.2)	0	(0.0)	1	(0.1)
Neutropenia	1	(0.2)	1	(0.4)	2	(0.3)
Cardiac Disorders	1	(0.2)	0	(0.0)	1	(0.1)
Myocardial Infarction	1	(0.2)	0	(0.0)	1	(0.1)
Gastrointestinal Disorders	1	(0.2)	1	(0.4)	2	(0.3)
Gastritis	1	(0.2)	0	(0.0)	1	(0.1)
Pancreatitis	0	(0.0)	1	(0.4)	1	(0.1)
Hepatobiliary Disorders	1	(0.2)	0	(0.0)	1	(0.1)
Hepatitis	1	(0.2)	0	(0.0)	1	(0.1)
Immune System Disorders	2	(0.4)	0	(0.0)	2	(0.3)
Drug Hypersensitivity	1	(0.2)	0	(0.0)	1	(0.1)
Hypersensitivity	2	(0.4)	0	(0.0)	2	(0.3)
Metabolism And Nutrition Disorders	0	(0.0)	1	(0.4)	1	(0.1)
Hyperglycaemia	0	(0.0)	1	(0.4)	1	(0.1)
Nervous System Disorders	0	(0.0)	1	(0.4)	1	(0.1)
Lacunar Infarction	0	(0.0)	1	(0.4)	1	(0.1)
Renal And Urinary Disorders	2	(0.4)	1	(0.4)	3	(0.4)
Nephrolithiasis	0	(0.0)	1	(0.4)	1	(0.1)
Nephropathy Toxic	1	(0.2)	0	(0.0)	1	(0.1)

Number (%) of Patients With Specific Serious and Drug-Related (Overall) Clinical Adverse Experiences (Incidence >0% in One or More Treatment Groups) by System Organ Class—Treatment-Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019)
- Original Application

	MK-0518 400 mg b.i.d. (N = 507)		Placebo (N = 282)		Total (N = 789)	
	n	(%)	n	(%)	n	(%)
Renal And Urinary Disorders	2	(0.4)	1	(0.4)	3	(0.4)
Renal Failure	1	(0.2)	0	(0.0)	1	(0.1)
Skin And Subcutaneous Tissue Disorders	0	(0.0)	1	(0.4)	1	(0.1)
Lipoatrophy	0	(0.0)	1	(0.4)	1	(0.1)

Although a patient may have had two or more serious and drug-related clinical adverse experiences, the patient is counted only once within a category. The same patient may appear in different categories.

Note: MK-0518 and Placebo were administered with Optimized Background Therapy (OBT).

Adverse experience terms are from MedDRA Version 9.1

[Ref. 5.3.5.1: P005, P018, P019]

Appendix 2.7.4: 50

Listing of Patients With Serious Clinical Adverse Experiences -Treatment-Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Cumulative Data*

Study Number	AN	Gen-der	Race	Age	Period	Therapy	Total Daily Dose	Rela-tive Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontin-uance†	Intensity	Ser-ious	Drug Relation-ship	Action Taken	Outcome
MK-0518 400 mg b.i.d.																
0050001	3232	M	Hispa	52 yr	Dose-Ranging	MK-0518	800.00 mg	10	Irritable bowel syndrome	2 day	518	severe	Y	def not	no action with test drug	recovered
	3265	M	Hispa	35 yr	Dose-Ranging	Off Drug 1 day		78	Cholecystitis	7 day	588	severe	Y	def not	interrupted PRx	recovered
0050011	3880	M	Hispa	43 yr	Dose-Ranging	MK-0518	800.00 mg	65	Pneumonia	6 day	482	severe	Y	def not	no action with test drug	recovered
0050021	3876	M	white	48 yr	Dose-Ranging	MK-0518	800.00 mg	209	Coronary artery disease	5.49 mo	375	severe	Y	prob not	no action with test drug	recovered
0050023	3866	M	white	32 yr	Dose-Ranging	MK-0518	800.00 mg	124	Staphylococcal infection	5 day	438	severe	Y	def not	no action with test drug	recovered
0050030	2979	M	white	50 yr	Dose-Ranging	MK-0518	800.00 mg	308	Herpes simplex	8 day	586	mod	Y	def not	no action with test drug	recovered
0050031	3274	M	white	41 yr	Dose-Ranging	MK-0518	800.00 mg	91	Interstitial lung disease	1.28 mo	346	mild	Y	def not	no action with test drug	recovered
Placebo																

Listing of Patients With Serious Clinical Adverse Experiences -Treatment-Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Cumulative Data*

Study Number	AN	Gender	Race	Age	Period	Therapy	Total Daily Dose	Relative Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontinuance†	Intensity	Serious	Drug Relationship	Action Taken	Outcome
Placebo																
0050009	3272	M	black	43 yr	Dose-Ranging	Placebo	0.00 mg	61	Lacunar infarction	NA	594		Y	poss	no action with test drug	NA
0050021	3225	M	white	46 yr	Dose-Ranging	Placebo	0.00 mg	121	Tracheobronchitis	7 day	469	severe	Y	def not	no action with test drug	recovered
0050022	3278	M	white	51 yr	Dose-Ranging	Placebo	0.00 mg	146	Lipoatrophy	CONT	181	severe	Y	poss	discontinued PRx	not recovered
MK-0518 400 mg b.i.d.																
0180003	**8269**	**F**	**Asian**	**63 yr**	**Double-Blind**	**MK-0518**	**800.00 mg**	**222**	**Pneumonia**	**CONT**	**229**	**mod**	**Y**	**def not**	**no action with test drug**	**not recovered**
0180004	8256	M	white	46 yr	Double-Blind	MK-0518	800.00 mg	110	**Kaposi's sarcoma AIDS related**	5.59 mo	217	mod	Y	def not	no action with test drug	recovered
	8321	M	white	46 yr	Double-Blind	MK-0518	800.00 mg	35	Squamous cell carcinoma	6.31 mo	230	mod	Y	prob not	no action with test drug	recovered

Listing of Patients With Serious Clinical Adverse Experiences -Treatment-Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Cumulative Data*

Study Number	AN	Gender	Race	Age	Period	Therapy	Total Daily Dose	Relative Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontinuance†	Intensity	Serious	Drug Relationship	Action Taken	Outcome
MK-0518 400 mg b.i.d.																
0180004	**8391**	**M**	**white**	**47 yr**	**Double-Blind**	**MK-0518**	**800.00 mg**	**129**	**Portal hypertension**	**CONT**	**164**	**mod**	**Y**	**prob not**	**no action with test drug**	**not recovered**
						MK-0518	**800.00 mg**	**129**	**Varices oesophageal**	**CONT**	**164**	**severe**	**Y**	**def not**	**no action with test drug**	**not recovered**
0180007	8318	M	white	51 yr	Double-Blind	MK-0518	800.00 mg	1	Nephropathy toxic	2.27 mo	225	severe	Y	prob	no action with test drug	recovered
						MK-0518	800.00 mg	1	Weight decreased	2.27 mo	225	severe	Y	prob not	no action with test drug	recovered
0180008	**8385**	**M**	**black**	**47 yr**	**Double-Blind**	**MK-0518**	**800.00 mg**	**134**	**Herpes simplex**	**CONT**	**174**	**mod**	**Y**	**poss**	**no action with test drug**	**not recovered**
0180011	8287	F	white	61 yr	Double-Blind	MK-0518	1600.00 mg	1	Overdose	15 day	252	mod	Y	def not	no action with test drug	recovered
	8348	M	white	48 yr	Double-Blind	MK-0518	800.00 mg	55	Humerus fracture	CONT	224	severe	Y	def not	no action with test drug	not recovered

Listing of Patients With Serious Clinical Adverse Experiences -Treatment-Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Cumulative Data*

Study Number	AN	Gen-der	Race	Age	Period	Therapy	Total Daily Dose	Rela-tive Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontin-uance†	Intensity	Ser-ious	Drug Relation-ship	Action Taken	Outcome
MK-0518 400 mg b.i.d.																
0180011	8363	M	white	53 yr	Double-Blind	MK-0518	800.00 mg	128	Myocardial infarction	10 day	164	severe	Y	prob not	no action with test drug	recovered
						MK-0518	800.00 mg	137	Angina pectoris	12 day	164	severe	Y	prob not	no action with test drug	recovered
0180014	**7067**	**M**	**white**	**43 yr**	**Double-Blind**	**MK-0518**	**800.00 mg**	**223**	**Appendicitis**	**5 day**	**236**	**mod**	**Y**	**def not**	**interrupted PRx**	**recovered**
	8292	F	white	60 yr	Double-Blind	MK-0518	800.00 mg	27	Rectal cancer	CONT	215	severe	Y	def not	no action with test drug	not recovered
	8345	M	white	42 yr	Double-Blind	MK-0518	800.00 mg	129	Pneumonia pneumococcal	9 day	224	mod	Y	def not	no action with test drug	recovered
						MK-0518	800.00 mg	129	Renal failure chronic	3.19 mo	224	severe	Y	def	interrupted PRx	recovered
						MK-0518	800.00 mg	129	Renal tubular necrosis	3.19 mo	224	severe	Y	def	interrupted PRx	recovered
0180017	**8250**	**M**	**white**	**51 yr**	**Double-Blind**	**Off Drug 54 days**		**273**	**Chest pain**	**CONT**	**219**	**mod**	**Y**	**prob not**	**no action with test drug**	**not recovered**

Listing of Patients With Serious Clinical Adverse Experiences -Treatment-Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Cumulative Data*

Study Number	AN	Gender	Race	Age	Period	Therapy	Total Daily Dose	Relative Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontinuance†	Intensity	Serious	Drug Relationship	Action Taken	Outcome
MK-0518 400 mg b.i.d.																
0180021	7115	M	white	55 yr	Double-Blind	MK-0518	800.00 mg	27	Cholangitis	1.54 mo	168	severe	Y	def not	no action with test drug	recovered
0180023	7021	M	white	44 yr	Double-Blind	MK-0518	800.00 mg	225	**Choriomeningitis lymphocytic**	6 day	280	mod	Y	prob not	no action with test drug	recovered
0180027	8372	M	white	49 yr	Double-Blind	MK-0518	800.00 mg	109	Myocardial infarction	7 day	189	mod	Y	poss	no action with test drug	recovered
						MK-0518	800.00 mg	119	Myocardial infarction	9 day	189	mod	Y	poss	no action with test drug	recovered
0180030	6404	M	black	62 yr	Double-Blind	MK-0518	800.00 mg	23	Hypersensitivity	10 day	222	severe	Y	prob	interrupted PRx	recovered
						MK-0518	800.00 mg	33	Drug hypersensitivity	3 day	222	severe	Y	def	interrupted PRx	recovered
						Off Drug 1 day		38	Hypersensitivity	28 day	222	severe	Y	prob	interrupted PRx	recovered
						Off Drug 29 days		66	Benign prostatic hyperplasia	24 day	222	severe	Y	def not	no action with test drug	recovered

Listing of Patients With Serious Clinical Adverse Experiences -Treatment-Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Cumulative Data*

Study Number	AN	Gender	Race	Age	Period	Therapy	Total Daily Dose	Relative Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontinuance†	Intensity	Serious	Drug Relationship	Action Taken	Outcome
MK-0518 400 mg b.i.d.																
0180030	6404	M	black	62 yr	Double-Blind	Off Drug 30 days		67	Oedema peripheral	4.57 mo	222	mod	Y	def not	no action with test drug	recovered
						MK-0518	800.00 mg	127	Upper gastrointestinal haemorrhage	18 hr	222	severe	Y	prob not	interrupted PRx	recovered
						Off Drug 13 days		167	Abdominal pain	4 day	222	severe	Y	def not	no action with test drug	recovered
0180032	8325	F	black	40 yr	Double-Blind	MK-0518	800.00 mg	26	Hyperthyroidism	1.12 mo	108	severe	Y	prob not	interrupted PRx	recovered
						MK-0518	800.00 mg	30	Hepatitis	15 day	108	mod	Y	poss	interrupted PRx	recovered
						MK-0518	800.00 mg	102	Bronchopneumonia	CONT	108	severe	Y	def not	no action with test drug	fatal
						MK-0518	800.00 mg	102	Hepatitis	CONT	108	severe	Y	poss	discontinued PRx	not recovered
					Post-Treatment DB	Off Drug 10 days		118	Rectal haemorrhage	CONT	108	severe	Y	def not	no action with test drug	fatal

Listing of Patients With Serious Clinical Adverse Experiences -Treatment-Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Cumulative Data*

Study Number	AN	Gen-der	Race	Age	Period	Therapy	Total Daily Dose	Rela-tive Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontin-uance†	Intensity	Ser-ious	Drug Relation-ship	Action Taken	Outcome
MK-0518 400 mg b.i.d.																
0180032	8325	F	black	40 yr	Post-Treatment DB	Off Drug 11 days		119	Septic shock	CONT	108	severe	Y	def not	no action with test drug	fatal
0180033	7086	M	white	45 yr	Double-Blind	Off Drug 2 days		23	Gastritis	3 day	224	severe	Y	prob	interrupted PRx	recovered
						Off Drug 3 days		**211**	**Gastritis**	**4 day**	**224**	**mod**	**Y**	**prob**	**interrupted PRx**	**recovered**
0180036	8353	M	multi	38 yr	Double-Blind	MK-0518	800.00 mg	27	Malaise	6 day	80	mod	Y	def not	interrupted PRx	recovered
						MK-0518	800.00 mg	76	Meningitis cryptococcal	16 day	80	mod	Y	def not	discontinued PRx	fatal
0180041	7026	M	white	42 yr	Double-Blind	MK-0518	800.00 mg	29	**Kaposi's sarcoma AIDS related**	6.37 mo	278	mild	Y	def not	no action with test drug	recovered
	7031	M	white	40 yr	Double-Blind	MK-0518	800.00 mg	221	Lower limb fracture	CONT	240	mod	Y	def not	no action with test drug	not recovered
	7033	M	white	62 yr	Double-Blind	MK-0518	800.00 mg	125	Incisional hernia	1 day	278	severe	Y	def not	no action with test drug	recovered
0180044	7036	M	white	53 yr	Double-Blind	MK-0518	800.00 mg	108	Pneumonia	27 day	279	mod	Y	def not	no action with test drug	recovered

Listing of Patients With Serious Clinical Adverse Experiences -Treatment-Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Cumulative Data*

Study Number	AN	Gender	Race	Age	Period	Therapy	Total Daily Dose	Relative Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontinuance†	Intensity	Serious	Drug Relationship	Action Taken	Outcome
MK-0518 400 mg b.i.d.																
0180047	**7123**	**M**	**white**	**56 yr**	**Double-Blind**	**MK-0518**	**800.00 mg**	**7**	**HIV infection**	**15 day**	**179**	**mild**	**Y**	**def not**	**no action with test drug**	**recovered**
0180051	8335	M	white	51 yr	Double-Blind	MK-0518	800.00 mg	21	Pyrexia	8 day	223	mod	Y	prob not	no action with test drug	recovered
0180054	**7019**	**M**	**white**	**44 yr**	**Double-Blind**	**MK-0518**	**800.00 mg**	**208**	**Nephrotic syndrome**	**CONT**	**237**	**mild**	**Y**	**prob not**	**no action with test drug**	**not recovered**
						MK-0518	**800.00 mg**	**209**	**Focal glomerulosclerosis**	**CONT**	**237**	**mild**	**Y**	**prob not**	**no action with test drug**	**not recovered**
0180057	7601	M	black	47 yr	Double-Blind	MK-0518	800.00 mg	226	Spinal fracture	CONT	280	severe	Y	def not	no action with test drug	not recovered
	8241	F	white	43 yr	Double-Blind	MK-0518	800.00 mg	9	Sinusitis	14 day	280	mod	Y	prob not	no action with test drug	recovered
						MK-0518	800.00 mg	97	Endophthalmitis	9 day	280	severe	Y	prob not	no action with test drug	recovered

Listing of Patients With Serious Clinical Adverse Experiences -Treatment-Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Cumulative Data*

Study Number	AN	Gender	Race	Age	Period	Therapy	Total Daily Dose	Relative Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontinuance†	Intensity	Serious	Drug Relationship	Action Taken	Outcome
MK-0518 400 mg b.i.d.																
0180057	8241	F	white	43 yr	Double-Blind	MK-0518	800.00 mg	133	Endophthalmitis	9 day	280	severe	Y	prob not	no action with test drug	recovered
						MK-0518	**800.00 mg**	**239**	**Haemolytic anaemia**	**CONT**	**280**	**severe**	**Y**	**prob not**	**no action with test drug**	**not recovered**
0180058	7005	M	white	60 yr	Double-Blind	MK-0518	800.00 mg	76	B-cell lymphoma	CONT	280	severe	Y	prob not	no action with test drug	not recovered
						MK-0518	800.00 mg	119	Septic shock	4 day	280	severe	Y	def not	no action with test drug	recovered
						MK-0518	800.00 mg	233	Prostatitis	2.92 mo	280	severe	Y	def not	no action with test drug	recovered
						MK-0518	800.00 mg	234	Cytomegalovirus infection	1.51 mo	280	severe	Y	def not	no action with test drug	recovered
0180059	7014	F	black	44 yr	Double-Blind	MK-0518	800.00 mg	24	**Choriomeningitis lymphocytic**	CONT	308	severe	Y	def not	no action with test drug	not recovered

Listing of Patients With Serious Clinical Adverse Experiences -Treatment-Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Cumulative Data*

Study Number	AN	Gender	Race	Age	Period	Therapy	Total Daily Dose	Relative Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontinuance†	Intensity	Serious	Drug Relationship	Action Taken	Outcome
MK-0518 400 mg b.i.d.																
0180059	7014	F	black	44 yr	Double-Blind	MK-0518	800.00 mg	59	Encephalitis	CONT	308	severe	Y	prob not	no action with test drug	not recovered
	8204	M	white	45 yr	Double-Blind	MK-0518	800.00 mg	71	Pericarditis	24 day	93	mild	Y	prob not	no action with test drug	recovered
						MK-0518	800.00 mg	74	Mycobacterial infection	21 day	93	severe	Y	def not	discontinued PRx	fatal
						MK-0518	800.00 mg	85	**T-cell lymphoma**	10 day	93	severe	Y	prob not	discontinued PRx	fatal
						MK-0518	800.00 mg	93	Multi-organ failure	2 day	93	severe	Y	def not	discontinued PRx	fatal
						MK-0518	800.00 mg	93	Shock	2 day	93	severe	Y	def not	discontinued PRx	fatal
0180060	8230	F	black	42 yr	Double-Blind	MK-0518	800.00 mg	34	Pneumonia	14 day	280	mod	Y	def not	no action with test drug	recovered

Listing of Patients With Serious Clinical Adverse Experiences -Treatment-Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Cumulative Data*

Study Number	AN	Gender	Race	Age	Period	Therapy	Total Daily Dose	Relative Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontinuance†	Intensity	Serious	Drug Relationship	Action Taken	Outcome
Placebo																
0180005	7045	M	white	44 yr	Double-Blind	Placebo	0.00 mg	189	Gallbladder disorder	CONT	218	mod	Y	def not	no action with test drug	not recovered
						Off Drug 51 days		**269**	**Oedema genital**	**CONT**	**218**	**severe**	**Y**	**def not**	**no action with test drug**	**not recovered**
0180008	8266	M	white	51 yr	Double-Blind	Placebo	0.00 mg	5	Pneumonia	25 day	25	severe	Y	def not	discontinued PRx	fatal
	8377	M	white	58 yr	Double-Blind	Placebo	0.00 mg	32	Osteoporotic fracture	CONT	173	mod	Y	prob not	no action with test drug	not recovered
						Placebo	0.00 mg	72	Thoracic vertebral fracture	CONT	173	mod	Y	prob not	no action with test drug	not recovered
						Placebo	**0.00 mg**	**135**	**Malnutrition**	**CONT**	**173**	**mod**	**Y**	**prob not**	**no action with test drug**	**not recovered**
						Placebo	**0.00 mg**	**135**	**Panic attack**	**CONT**	**173**	**mod**	**Y**	**prob not**	**no action with test drug**	**not recovered**

Listing of Patients With Serious Clinical Adverse Experiences -Treatment-Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Cumulative Data*

Study Number	AN	Gender	Race	Age	Period	Therapy	Total Daily Dose	Relative Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontinuance†	Intensity	Serious	Drug Relationship	Action Taken	Outcome
Placebo																
0180008	8377	M	white	58 yr	Double-Blind	**Placebo**	**0.00 mg**	**135**	**Poor quality sleep**	**CONT**	**173**	**mod**	**Y**	**prob not**	**no action with test drug**	**not recovered**
0180012	8234	M	white	42 yr	Double-Blind	Placebo	0.00 mg	59	Leukopenia	29 day	280	mild	Y	prob not	no action with test drug	recovered
						Placebo	0.00 mg	71	Convulsion	1 day	280	mild	Y	prob not	no action with test drug	recovered
						Placebo	0.00 mg	71	Hypotension	1 day	280	mild	Y	prob not	no action with test drug	recovered
						Placebo	0.00 mg	71	Pseudomonal sepsis	17 day	280	mild	Y	def not	no action with test drug	recovered
						Placebo	0.00 mg	71	Septic shock	17 day	280	severe	Y	prob not	no action with test drug	recovered
						Placebo	0.00 mg	116	Epilepsy	1 day	280	mild	Y	prob not	no action with test drug	recovered

Listing of Patients With Serious Clinical Adverse Experiences -Treatment-Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Cumulative Data*

Study Number	AN	Gender	Race	Age	Period	Therapy	Total Daily Dose	Relative Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontinuance†	Intensity	Serious	Drug Relationship	Action Taken	Outcome
Placebo																
0180012	8234	M	white	42 yr	Double-Blind	Placebo	0.00 mg	117	Leukopenia	CONT	280	mild	Y	prob not	no action with test drug	not recovered
						Placebo	0.00 mg	124	Oesophageal candidiasis	1.58 mo	280	mild	Y	def not	no action with test drug	recovered
						Placebo	0.00 mg	126	Pneumonia	13 day	280	mild	Y	prob not	no action with test drug	recovered
						Placebo	0.00 mg	137	Uveitis	1.22 mo	280	mild	Y	prob not	no action with test drug	recovered
						Placebo	**0.00 mg**	**232**	**Epilepsy**	**1 day**	**280**	**mild**	**Y**	**prob not**	**no action with test drug**	**recovered**
						Placebo	**0.00 mg**	**232**	**Pyrexia**	**2 day**	**280**	**mild**	**Y**	**prob not**	**no action with test drug**	**recovered**
						Placebo	**0.00 mg**	**240**	**Pyrexia**	**11 day**	**280**	**mild**	**Y**	**prob not**	**no action with test drug**	**recovered**

Listing of Patients With Serious Clinical Adverse Experiences -Treatment-Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Cumulative Data*

Study Number	AN	Gender	Race	Age	Period	Therapy	Total Daily Dose	Relative Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontinuance†	Intensity	Serious	Drug Relationship	Action Taken	Outcome
Placebo																
0180012	8234	M	white	42 yr	Double-Blind	**Placebo**	**0.00 mg**	**257**	**Epilepsy**	**1 day**	**280**	**mild**	**Y**	**prob not**	**no action with test drug**	**recovered**
						Placebo	**0.00 mg**	**257**	**Pneumonia**	**11 day**	**280**	**mild**	**Y**	**prob not**	**no action with test drug**	**recovered**
						Placebo	**0.00 mg**	**257**	**Pyrexia**	**2 day**	**280**	**mild**	**Y**	**prob not**	**no action with test drug**	**recovered**
						Placebo	**0.00 mg**	**257**	**Septic shock**	**1 day**	**280**	**mild**	**Y**	**prob not**	**no action with test drug**	**recovered**
0180014	7091	F	white	36 yr	Double-Blind	Placebo	0.00 mg	39	Varicophlebitis	4 day	168	mod	Y	def not	no action with test drug	recovered
	8323	M	white	19 yr	Double-Blind	Placebo	0.00 mg	19	Oesophageal candidiasis	10 day	235	mod	Y	def not	no action with test drug	recovered
0180018	7098	M	white	47 yr	Double-Blind	Placebo	0.00 mg	105	Vertigo	12 day	202	mod	Y	def not	no action with test drug	recovered

Listing of Patients With Serious Clinical Adverse Experiences -Treatment-Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Cumulative Data*

Study Number	AN	Gen-der	Race	Age	Period	Therapy	Total Daily Dose	Rela-tive Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontin-uance†	Intensity	Ser-ious	Drug Relation-ship	Action Taken	Outcome
Placebo																
0180020	8343	M	white	36 yr	Double-Blind	Placebo	0.00 mg	58	Intervertebral disc protrusion	3.98 mo	220	mod	Y	def not	no action with test drug	recovered
0180021	**7095**	**M**	**white**	**43 yr**	**Double-Blind**	**Placebo**	**0.00 mg**	**169**	**Hepatitis toxic**	**13 day**	**224**	**mod**	**Y**	**def**	**no action with test drug**	**recovered**
0180023	7024	M	white	57 yr	Double-Blind	Placebo	0.00 mg	119	Nephropathy	CONT	290	mod	Y	prob not	no action with test drug	not recovered
						Placebo	0.00 mg	177	Pulmonary hypertension	CONT	290	severe	Y	prob not	no action with test drug	not recovered
0180024	8219	M	white	45 yr	Double-Blind	Off Drug 1 day		51	Rectal stenosis	17 day	295	mod	Y	def not	no action with test drug	recovered
0180041	**8228**	**M**	**white**	**43 yr**	**Double-Blind**	**Off Drug 1 day**		**272**	**Gynaecomastia**	**2 day**	**271**	**mod**	**Y**	**def not**	**no action with test drug**	**recovered**
0180045	8212	M	white	40 yr	Double-Blind	Placebo	0.00 mg	145	Hypoacusis	4 day	276	severe	Y	def not	no action with test drug	recovered

Listing of Patients With Serious Clinical Adverse Experiences -Treatment-Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Cumulative Data*

Study Number	AN	Gender	Race	Age	Period	Therapy	Total Daily Dose	Relative Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontinuance†	Intensity	Serious	Drug Relationship	Action Taken	Outcome
Placebo																
0180048	7605	M	white	45 yr	Double-Blind	Off Drug 1 day		109	Psychomotor hyperactivity	8 day	255	mod	Y	def not	interrupted PRx	recovered
0180051	8299	M	white	43 yr	Double-Blind	Placebo	0.00 mg	85	Asthenia	3.09 mo	246	mod	Y	prob not	no action with test drug	recovered
	8402	M	white	43 yr	Double-Blind	Off Drug 25 days		105	Depression	8 day	187	severe	Y	prob not	no action with test drug	recovered
						Placebo	**0.00 mg**	**158**	**Intentional overdose**	**5 day**	**187**	**severe**	**Y**	**prob not**	**no action with test drug**	**recovered**
0180059	8206	M	white	41 yr	Double-Blind	Placebo	0.00 mg	113	Cytomegalovirus colitis	3.45 mo	301	severe	Y	def not	no action with test drug	recovered
						Placebo	0.00 mg	113	Oral candidiasis	1.41 mo	301	severe	Y	def not	no action with test drug	recovered
0180062	8346	M	white	50 yr	Double-Blind	Placebo	0.00 mg	29	Neutropenia	CONT	216	mod	Y	prob not	no action with test drug	not recovered

Listing of Patients With Serious Clinical Adverse Experiences -Treatment-Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Cumulative Data*

Study Number	AN	Gender	Race	Age	Period	Therapy	Total Daily Dose	Relative Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontinuance†	Intensity	Serious	Drug Relationship	Action Taken	Outcome
Placebo																
0180062	8346	M	white	50 yr	Double-Blind	Placebo	0.00 mg	57	Erythema infectiosum	CONT	216	mod	Y	prob not	interrupted PRx	not recovered
MK-0518 400 mg b.i.d.																
0190002	16314	M	Hispa	58 yr	Post-Treatment DB	Off Drug 1 day		32	**Aspergillosis**	19 day	31	severe	Y	prob not	no action with test drug	fatal
						Off Drug 1 day		32	Dehydration	CONT	31	mod	Y	prob not	discontinued PRx	not recovered
						Off Drug 1 day		32	**Tuberculosis**	19 day	31	severe	Y	prob not	no action with test drug	fatal
0190003	**16248**	**M**	**white**	**41 yr**	**Double-Blind**	**Off Drug 1 day**		**225**	**Abdominal pain**	**1.08 mo**	**224**	**mod**	**Y**	**def not**	**no action with test drug**	**recovered**
0190006	15028	M	white	46 yr	Double-Blind	MK-0518	800.00 mg	62	Neuralgia	CONT	62	severe	Y	def not	no action with test drug	not recovered

Listing of Patients With Serious Clinical Adverse Experiences -Treatment-Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Cumulative Data*

Study Number	AN	Gender	Race	Age	Period	Therapy	Total Daily Dose	Relative Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontinuance†	Intensity	Serious	Drug Relationship	Action Taken	Outcome
MK-0518 400 mg b.i.d.																
0190006	15028	M	white	46 yr	Post-Treatment DB	Off Drug 2 days		64	Lymphoma	5 day	62	severe	Y	def not	no action with test drug	fatal
	16306	M	white	43 yr	Double-Blind	MK-0518	800.00 mg	25	Small intestinal obstruction	8 day	209	mod	Y	prob not	interrupted PRx	recovered
						MK-0518	800.00 mg	57	Small intestinal obstruction	8 day	209	mod	Y	prob not	interrupted PRx	recovered
0190008	15098	M	white	46 yr	Double-Blind	MK-0518	800.00 mg	77	Viral infection	10 day	161	severe	Y	prob not	interrupted PRx	recovered
0190010	16279	M	black	47 yr	Double-Blind	MK-0518	800.00 mg	8	Cellulitis	7 day	267	severe	Y	def not	no action with test drug	recovered
0190011	15084	M	white	63 yr	Double-Blind	MK-0518	800.00 mg	25	**Rectal cancer stage 0**	CONT	221	mild	Y	def not	no action with test drug	not recovered
0190013	16278	M	Hispa	44 yr	Double-Blind	Off Drug 1 day		119	Pneumonia	9 day	227	severe	Y	def not	no action with test drug	recovered
0190016	15129	M	black	58 yr	Double-Blind	MK-0518	400.00 mg	42	Anaemia	1.45 mo	171	mod	Y	def	interrupted PRx	recovered
						MK-0518	400.00 mg	42	Neutropenia	3 day	171	mild	Y	def	interrupted PRx	recovered

Listing of Patients With Serious Clinical Adverse Experiences -Treatment-Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Cumulative Data*

Study Number	AN	Gen-der	Race	Age	Period	Therapy	Total Daily Dose	Rela-tive Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontin-uance†	Intensity	Ser-ious	Drug Relation-ship	Action Taken	Outcome
MK-0518 400 mg b.i.d.																
0190018	16228	M	white	48 yr	Double-Blind	Off Drug 2 days		221	Asthma	CONT	219	mod	Y	def not	no action with test drug	not recovered
						Off Drug 2 days		221	Cardiac failure congestive	CONT	219	mod	Y	def not	no action with test drug	not recovered
0190019	15006	M	white	37 yr	Double-Blind	MK-0518	800.00 mg	83	Nausea	6 day	86	severe	Y	prob not	no action with test drug	recovered
						MK-0518	400.00 mg	86	Vomiting	3 day	86	severe	Y	prob not	no action with test drug	recovered
	15100	M	white	48 yr	Double-Blind	MK-0518	400.00 mg	45	Hypersensitivity	10 day	118	severe	Y	def	interrupted PRx	recovered
						Off Drug 19 days		64	**Retroviral infection**	8 day	118	mod	Y	def not	no action with test drug	recovered
						Off Drug 32 days		77	Anaemia	12 day	118	severe	Y	prob not	no action with test drug	recovered
						MK-0518	800.00 mg	85	Depression	5 day	118	severe	Y	prob not	no action with test drug	recovered

Listing of Patients With Serious Clinical Adverse Experiences -Treatment-Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Cumulative Data*

Study Number	AN	Gender	Race	Age	Period	Therapy	Total Daily Dose	Relative Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontinuance†	Intensity	Serious	Drug Relationship	Action Taken	Outcome
MK-0518 400 mg b.i.d.																
0190019	15100	M	white	48 yr	Double-Blind	MK-0518	800.00 mg	98	Dehydration	10 day	118	mod	Y	def not	no action with test drug	recovered
						MK-0518	800.00 mg	98	Syncope	10 day	118	mod	Y	def not	no action with test drug	recovered
						MK-0518	800.00 mg	101	Anaemia	1 day	118	severe	Y	def not	no action with test drug	recovered
0190023	16296	M	white	43 yr	Double-Blind	MK-0518	800.00 mg	160	Infection	CONT	228	mod	Y	def not	no action with test drug	not recovered
0190026	16347	M	white	48 yr	Double-Blind	MK-0518	800.00 mg	48	Pneumonia	15 day	167	severe	Y	def not	interrupted PRx	recovered
						Off Drug 39 days		88	Deep vein thrombosis	1.54 mo	167	mod	Y	def not	no action with test drug	recovered
						Off Drug 57 days		106	Oesophageal candidiasis	CONT	167	mod	Y	def not	no action with test drug	not recovered
						MK-0518	800.00 mg	132	Pneumonia	18 day	167	mod	Y	def not	no action with test drug	recovered

Listing of Patients With Serious Clinical Adverse Experiences -Treatment-Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Cumulative Data*

Study Number	AN	Gender	Race	Age	Period	Therapy	Total Daily Dose	Relative Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontinuance†	Intensity	Serious	Drug Relationship	Action Taken	Outcome
MK-0518 400 mg b.i.d.																
0190026	16347	M	white	48 yr	Double-Blind	**Off Drug 22 days**		**189**	**Pneumonia**	**23 day**	**167**	**mod**	**Y**	**def not**	**no action with test drug**	**recovered**
						Off Drug 54 days		**221**	**Pneumonia**	**16 day**	**167**	**mod**	**Y**	**def not**	**no action with test drug**	**recovered**
0190027	**15113**	**M**	**black**	**41 yr**	**Double-Blind**	**MK-0518**	**800.00 mg**	**30**	**Mass**	**4.40 mo**	**174**	**mild**	**Y**	**prob not**	**no action with test drug**	**recovered**
	16365	M	black	48 yr	Double-Blind	MK-0518	800.00 mg	67	Squamous cell carcinoma	1.94 mo	164	severe	Y	prob not	no action with test drug	recovered
						MK-0518	800.00 mg	83	Presyncope	CONT	164	severe	Y	prob not	no action with test drug	not recovered
0190029	**15082**	**M**	**black**	**45 yr**	**Double-Blind**	**MK-0518**	**800.00 mg**	**203**	**Convulsion**	**1 day**	**235**	**mod**	**Y**	**def not**	**no action with test drug**	**recovered**
	16239	M	Hispa	47 yr	Double-Blind	MK-0518	800.00 mg	51	Asthma	3 day	75	mod	Y	def not	no action with test drug	recovered

Listing of Patients With Serious Clinical Adverse Experiences -Treatment-Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Cumulative Data*

Study Number	AN	Gender	Race	Age	Period	Therapy	Total Daily Dose	Relative Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontinuance†	Intensity	Serious	Drug Relationship	Action Taken	Outcome
MK-0518 400 mg b.i.d.																
0190029	16239	M	Hispa	47 yr	Double-Blind	MK-0518	800.00 mg	56	Acinetobacter bacteraemia	CONT	75	mod	Y	def not	no action with test drug	not recovered
						MK-0518	800.00 mg	56	Immune reconstitution syndrome	CONT	75	mod	Y	def not	no action with test drug	not recovered
						MK-0518	800.00 mg	69	Hepatic neoplasm malignant	9 day	75	severe	Y	def not	discontinued PRx	fatal
0190031	16254	F	black	19 yr	Double-Blind	Off Drug 1 day		13	Bone pain	10 day	187	mod	Y	def not	interrupted PRx	recovered
						Off Drug 1 day		13	Malaise	10 day	187	mod	Y	def not	interrupted PRx	recovered
						Off Drug 1 day		13	Pyrexia	10 day	187	mod	Y	def not	interrupted PRx	recovered
						MK-0518	800.00 mg	74	Otitis media	5 day	187	mod	Y	def not	no action with test drug	recovered
						MK-0518	800.00 mg	86	Abscess bacterial	10 day	187	mod	Y	def not	no action with test drug	recovered

Listing of Patients With Serious Clinical Adverse Experiences -Treatment-Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Cumulative Data*

Study Number	AN	Gender	Race	Age	Period	Therapy	Total Daily Dose	Relative Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontinuance†	Intensity	Serious	Drug Relationship	Action Taken	Outcome
MK-0518 400 mg b.i.d.																
0190031	16254	F	black	19 yr	Double-Blind	MK-0518	800.00 mg	112	Subcutaneous abscess	11 day	187	mod	Y	def not	no action with test drug	recovered
						MK-0518	800.00 mg	114	Subcutaneous abscess	9 day	187	mod	Y	def not	no action with test drug	recovered
0190042	15115	M	black	39 yr	Double-Blind	MK-0518	800.00 mg	25	Renal failure	CONT	26	severe	Y	poss	discontinued PRx	not recovered
					Post-Treatment DB	Off Drug 12 days		38	Mental status changes	3 day	26	mod	Y	prob not	no action with test drug	recovered
	16335	M	white	40 yr	Double-Blind	Off Drug 1 day		9	Immune reconstitution syndrome	3.65 mo	195	mod	Y	prob not	interrupted PRx	recovered
						Off Drug 1 day		9	Meningitis cryptococcal	CONT	195	mod	Y	prob not	no action with test drug	not recovered
0190045	16318	M	white	50 yr	Double-Blind	MK-0518	800.00 mg	68	Cellulitis	17 day	200	mod	Y	prob not	no action with test drug	recovered

Listing of Patients With Serious Clinical Adverse Experiences -Treatment-Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Cumulative Data*

Study Number	AN	Gender	Race	Age	Period	Therapy	Total Daily Dose	Relative Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontinuance†	Intensity	Serious	Drug Relationship	Action Taken	Outcome
MK-0518 400 mg b.i.d.																
0190045	**16318**	**M**	**white**	**50 yr**	**Double-Blind**	**MK-0518**	**800.00 mg**	**197**	**Coronary artery disease**	**4 day**	**200**	**mod**	**Y**	**prob not**	**discontinued PRx**	**fatal**
0190046	15102	M	black	44 yr	Double-Blind	Off Drug 1 day		12	Dehydration	8 day	170	mild	Y	prob not	interrupted PRx	recovered
						Off Drug 1 day		12	Post procedural haemorrhage	8 day	170	mod	Y	prob not	interrupted PRx	recovered
0190048	**15067**	**M**	**white**	**51 yr**	**Double-Blind**	**Off Drug 1 day**		**233**	**Accidental overdose**	**1.18 mo**	**232**	**mild**	**Y**	**def**	**no action with test drug**	**recovered**
0190053	16323	M	white	45 yr	Double-Blind	MK-0518	800.00 mg	27	Depression	4.24 mo	132	severe	Y	prob not	no action with test drug	recovered
						Off Drug 1 day		81	Intentional overdose	3 day	132	severe	Y	def not	interrupted PRx	recovered
0190054	15090	M	white	45 yr	Double-Blind	MK-0518	800.00 mg	52	Cytomegalovirus colitis	CONT	172	severe	Y	def not	no action with test drug	not recovered
						MK-0518	800.00 mg	97	Pneumonia	1.22 mo	172	severe	Y	def not	no action with test drug	recovered

Listing of Patients With Serious Clinical Adverse Experiences -Treatment-Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Cumulative Data*

Study Number	AN	Gender	Race	Age	Period	Therapy	Total Daily Dose	Relative Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontinuance†	Intensity	Serious	Drug Relationship	Action Taken	Outcome
MK-0518 400 mg b.i.d.																
0190054	**15090**	**M**	**white**	**45 yr**	**Double-Blind**	**MK-0518**	**800.00 mg**	**140**	**Metastatic squamous cell carcinoma**	**CONT**	**172**	**severe**	**Y**	**def not**	**interrupted PRx**	**not recovered**
0190057	**14404**	**M**	**Hispa**	**31 yr**	**Double-Blind**	**Off Drug 11 days**		**182**	**Diarrhoea**	**4 day**	**171**	**mod**	**Y**	**prob not**	**interrupted PRx**	**recovered**
	14405	**M**	**Hispa**	**58 yr**	**Double-Blind**	**MK-0518**	**800.00 mg**	**149**	**Migraine**	**10 day**	**166**	**severe**	**Y**	**prob not**	**interrupted PRx**	**recovered**
Placebo																
0190002	16334	M	white	47 yr	Double-Blind	Placebo	0.00 mg	68	Migraine	3 day	183	severe	Y	prob not	no action with test drug	recovered
						Placebo	0.00 mg	68	Pyrexia	3 day	183	mod	Y	prob not	no action with test drug	recovered
0190003	15081	M	Hispa	44 yr	Double-Blind	Off Drug 1 day		36	Asthenia	7 day	215	mod	Y	prob not	interrupted PRx	recovered
						Off Drug 1 day		36	**Gastroenteritis**	7 day	215	mod	Y	def not	interrupted PRx	recovered
						Off Drug 1 day		36	Pyrexia	7 day	215	mod	Y	prob not	interrupted PRx	recovered

Listing of Patients With Serious Clinical Adverse Experiences -Treatment-Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Cumulative Data*

Study Number	AN	Gender	Race	Age	Period	Therapy	Total Daily Dose	Relative Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontinuance†	Intensity	Serious	Drug Relationship	Action Taken	Outcome
Placebo																
0190007	16299	M	white	49 yr	Double-Blind	Placebo	0.00 mg	140	AIDS dementia complex	CONT	199	mod	Y	def not	no action with test drug	not recovered
0190016	16237	F	black	41 yr	Double-Blind	Placebo	0.00 mg	66	Gastroenteritis cryptosporidial	7 day	272	mod	Y	def not	no action with test drug	recovered
						Placebo	0.00 mg	70	Cytomegalovirus chorioretinitis	CONT	272	mod	Y	def not	no action with test drug	not recovered
						Placebo	0.00 mg	103	Pneumonia	2.60 mo	272	severe	Y	def not	no action with test drug	recovered
						Placebo	0.00 mg	118	Gastroenteritis cryptosporidial	2.30 mo	272	mod	Y	def not	no action with test drug	recovered
	16260	F	black	54 yr	Double-Blind	Placebo	0.00 mg	13	Pyrexia	2 day	252	severe	Y	def not	interrupted PRx	recovered
0190017	16369	M	white	45 yr	Double-Blind	Placebo	0.00 mg	43	Hip fracture	6 day	168	severe	Y	def not	interrupted PRx	recovered
0190019	16223	M	white	38 yr	Double-Blind	Placebo	0.00 mg	117	**Atypical mycobacterial lymphadenitis**	5 day	279	mod	Y	prob not	no action with test drug	recovered

Listing of Patients With Serious Clinical Adverse Experiences -Treatment-Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Cumulative Data*

Study Number	AN	Gen-der	Race	Age	Period	Therapy	Total Daily Dose	Rela-tive Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontin-uance†	Intensity	Ser-ious	Drug Relation-ship	Action Taken	Outcome
Placebo																
0190022	15602	M	Hispa	40 yr	Double-Blind	Placebo	0.00 mg	111	Cytomegalovirus chorioretinitis	CONT	259	severe	Y	def not	no action with test drug	not recovered
	16313	M	Hispa	37 yr	Double-Blind	Placebo	0.00 mg	15	Oesophageal candidiasis	2.69 mo	71	mod	Y	def not	no action with test drug	recovered
0190024	15001	M	black	53 yr	Double-Blind	Placebo	0.00 mg	90	Anal fistula	2.40 mo	322	severe	Y	def not	no action with test drug	recovered
						Placebo	0.00 mg	90	Haemorrhoids	2.40 mo	322	severe	Y	def not	no action with test drug	recovered
	16201	M	black	53 yr	Double-Blind	Placebo	0.00 mg	33	Hyperglycaemia	15 day	307	severe	Y	poss	interrupted PRx	recovered
0190026	**16346**	**M**	**white**	**70 yr**	**Double-Blind**	**Off Drug 1 day**		**139**	**Pneumonia**	**17 day**	**165**	**mod**	**Y**	**def not**	**no action with test drug**	**recovered**
						Off Drug 56 days		**221**	**Infarction**	**CONT**	**165**	**mod**	**Y**	**def not**	**no action with test drug**	**not recovered**
0190030	15056	M	white	47 yr	Double-Blind	Placebo	0.00 mg	187	Coronary artery disease	9 day	224	severe	Y	def not	no action with test drug	recovered

Listing of Patients With Serious Clinical Adverse Experiences -Treatment-Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Cumulative Data*

Study Number	AN	Gender	Race	Age	Period	Therapy	Total Daily Dose	Relative Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontinuance†	Intensity	Serious	Drug Relationship	Action Taken	Outcome
Placebo																
0190031	16231	M	black	17 yr	Double-Blind	Placebo	0.00 mg	105	Salmonella bacteraemia	8 day	247	severe	Y	def not	no action with test drug	recovered
						Placebo	0.00 mg	127	Gastroenteritis salmonella	4 day	247	mod	Y	def not	no action with test drug	recovered
0190034	**15125**	**M**	**white**	**59 yr**	**Double-Blind**	**Off Drug 5 days**		**174**	**Endocarditis**	**CONT**	**169**	**mod**	**Y**	**prob not**	**no action with test drug**	**not recovered**
						Off Drug 15 days		**184**	**Renal failure**	**CONT**	**169**	**mod**	**Y**	**prob**	**interrupted PRx**	**not recovered**
	16389	M	multi	49 yr	Double-Blind	Placebo	0.00 mg	2	Nephrolithiasis	12 day	167	mod	Y	poss	no action with test drug	recovered
						Placebo	0.00 mg	105	Pancreatitis	20 day	167	mod	Y	poss	interrupted PRx	recovered
0190035	16377	M	white	54 yr	Double-Blind	Placebo	0.00 mg	115	Neutropenia	12 day	177	severe	Y	poss	no action with test drug	recovered
0190045	16407	M	black	60 yr	Double-Blind	Placebo	0.00 mg	70	Mitral valve incompetence	2 day	168	mod	Y	prob not	no action with test drug	recovered

Listing of Patients With Serious Clinical Adverse Experiences -Treatment-Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Cumulative Data*

Study Number	AN	Gender	Race	Age	Period	Therapy	Total Daily Dose	Relative Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontinuance[†]	Intensity	Serious	Drug Relationship	Action Taken	Outcome
Placebo																
0190051	15074	M	white	41 yr	Double-Blind	Placebo	0.00 mg	68	Myocardial infarction	5 day	225	mild	Y	prob not	no action with test drug	recovered

[†]Day study therapy was discontinued relative to the start of study therapy.
Drug Relationship: def = definitely, def not = definitely not, poss = possibly, prob = probably, prob not = probably not
Intensity: mod = moderate
Note: MK-0518 and Placebo were administered with Optimized Background Therapy (OBT).
Adverse experience terms are from MedDRA Version 9.1.

[Ref. 5.3.5.1: P005-Define, P018-Define, P019-Define]

Appendix 2.7.4: 51

Number (%) of Patients With Specific Serious Clinical Adverse Experiences (Incidence >0% in One or More Treatment Groups) by System Organ Class—Open-Label Post Virologic Failure Phase (Protocols 005, 018, and 019) - *Cumulative Data*

	MK-0518 (N = 223)	
	n	(%)
Patients With One Or More Adverse Experiences	27	(12.1)
Patients With No Adverse Experience	196	(87.9)
Blood And Lymphatic System Disorders	1	(0.4)
Bone Marrow Toxicity	1	(0.4)
Cardiac Disorders	1	(0.4)
Angina Unstable	1	(0.4)
Gastrointestinal Disorders	2	(0.9)
Diarrhoea	1	(0.4)
Oesophageal Varices Haemorrhage	1	(0.4)
General Disorders And Administration Site Conditions	3	(1.3)
Cyst	1	(0.4)
Fatigue	1	(0.4)
Pyrexia	1	(0.4)
Hepatobiliary Disorders	2	(0.9)
Cholecystitis Acute	1	(0.4)
Portal Hypertension	1	(0.4)
Immune System Disorders	1	(0.4)
Immune Reconstitution Syndrome	1	(0.4)
Infections And Infestations	11	(4.9)
Arthritis Bacterial	1	(0.4)
Cytomegalovirus Chorioretinitis	2	(0.9)

Number (%) of Patients With Specific Serious Clinical Adverse Experiences (Incidence >0% in One or More Treatment Groups) by System Organ Class—Open-Label Post Virologic Failure Phase (Protocols 005, 018, and 019) - *Cumulative Data*

	MK-0518 (N = 223)	
	n	(%)
Infections And Infestations	11	(4.9)
Gastroenteritis	1	(0.4)
Gastroenteritis Salmonella	1	(0.4)
Oesophageal Candidiasis	1	(0.4)
Pneumococcal Sepsis	1	(0.4)
Pneumocystis Jiroveci Pneumonia	1	(0.4)
Pneumonia	1	(0.4)
Progressive Multifocal Leukoencephalopathy	1	(0.4)
Sepsis	1	(0.4)
Septic Shock	1	(0.4)
Staphylococcal Abscess	1	(0.4)
Subcutaneous Abscess	1	(0.4)
Varicella	1	(0.4)
Injury, Poisoning And Procedural Complications	1	(0.4)
Accidental Overdose	1	(0.4)
Metabolism And Nutrition Disorders	1	(0.4)
Failure To Thrive	1	(0.4)
Neoplasms Benign, Malignant And Unspecified (Incl Cysts And Polyps)	3	(1.3)
Anal Cancer	1	(0.4)
Basal Cell Carcinoma	1	(0.4)
Hodgkin's Disease	2	(0.9)
Psychiatric Disorders	2	(0.9)

Number (%) of Patients With Specific Serious Clinical Adverse Experiences (Incidence >0% in One or More Treatment Groups) by System Organ Class—Open-Label Post Virologic Failure Phase (Protocols 005, 018, and 019) - *Cumulative Data*

	MK-0518 (N = 223)	
	n	(%)
Psychiatric Disorders	2	(0.9)
Depression	1	(0.4)
Suicidal Ideation	1	(0.4)
Reproductive System And Breast Disorders	1	(0.4)
Epididymitis	1	(0.4)
Respiratory, Thoracic And Mediastinal Disorders	2	(0.9)
Dyspnoea	1	(0.4)
Pleural Effusion	1	(0.4)
Skin And Subcutaneous Tissue Disorders	1	(0.4)
Henoch-Schonlein Purpura	1	(0.4)

Although a patient may have had two or more serious clinical adverse experiences, the patient is counted only once within a category. The same patient may appear in different categories.

Note: MK-0518 and Placebo were administered with Optimized Background Therapy (OBT).

Adverse experience terms are from MedDRA Version 9.1.

[Ref. 5.3.5.1: P005-Define, P018-Define, P019-Define]

Appendix 2.7.4: 52

Number (%) of Patients With Specific Serious Clinical Adverse Experiences (Incidence >0% in One or More Treatment Groups) by System Organ Class—Open-Label Post Virologic Failure Phase (Protocols 005, 018, and 019) - *Original Application*

	MK-0518 (N = 177)	
	n	(%)
Patients With One Or More Serious Adverse Experiences	19	(10.7)
Patients With No Serious Adverse Experience	158	(89.3)
Blood And Lymphatic System Disorders	1	(0.6)
Bone Marrow Toxicity	1	(0.6)
Cardiac Disorders	1	(0.6)
Angina Unstable	1	(0.6)
General Disorders And Administration Site Conditions	1	(0.6)
Fatigue	1	(0.6)
Hepatobiliary Disorders	2	(1.1)
Cholecystitis Acute	1	(0.6)
Portal Hypertension	1	(0.6)
Immune System Disorders	1	(0.6)
Immune Reconstitution Syndrome	1	(0.6)
Infections And Infestations	9	(5.1)
Arthritis Bacterial	1	(0.6)
Cytomegalovirus Chorioretinitis	2	(1.1)
Gastroenteritis Salmonella	1	(0.6)
Oesophageal Candidiasis	1	(0.6)
Pneumonia	1	(0.6)
Progressive Multifocal Leukoencephalopathy	1	(0.6)
Sepsis	1	(0.6)
Staphylococcal Infection	1	(0.6)

Number (%) of Patients With Specific Serious Clinical Adverse Experiences (Incidence >0% in One or More Treatment Groups) by System Organ Class—Open-Label Post Virologic Failure Phase (Protocols 005, 018, and 019) - *Original Application*

	MK-0518 (N = 177)	
	n	(%)
Infections And Infestations	9	(5.1)
Subcutaneous Abscess	1	(0.6)
Tuberculous Pleurisy	1	(0.6)
Varicella	1	(0.6)
Injury, Poisoning And Procedural Complications	1	(0.6)
Accidental Overdose	1	(0.6)
Metabolism And Nutrition Disorders	1	(0.6)
Failure To Thrive	1	(0.6)
Neoplasms Benign, Malignant And Unspecified (Incl Cysts And Polyps)	2	(1.1)
Basal Cell Carcinoma	1	(0.6)
Hodgkin's Disease	2	(1.1)
Psychiatric Disorders	1	(0.6)
Suicidal Ideation	1	(0.6)
Respiratory, Thoracic And Mediastinal Disorders	1	(0.6)
Dyspnoea	1	(0.6)
Skin And Subcutaneous Tissue Disorders	1	(0.6)
Henoch-Schonlein Purpura	1	(0.6)

Although a patient may have had two or more serious clinical adverse experiences, the patient is counted only once within a category. The same patient may appear in different categories.

Note: MK-0518 and Placebo were administered with Optimized Background Therapy (OBT).

Adverse experience terms are from MedDRA Version 9.1.

[Ref. 5.3.5.1: P005, P018, P019]

Appendix 2.7.4: 53

Listing of Patients With Serious Clinical Adverse Experiences—Open-Label Post Virologic Failure Phase
(Protocols 005, 018, and 019) - *Cumulative Data*

Study Number	AN	Gender	Race	Age	Period	Therapy	Total Daily Dose	Relative Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontinuance†	Intensity	Serious	Drug Relationship	Action Taken	Outcome
MK-0518																
0050005	**3871**	**M**	**white**	**38 yr**	**Post Viral Fail Optm**	**MK-0518**	**800.00 mg**	**373**	**Cyst**	**3 day**	**423**	**mod**	**Y**	**def not**	**no action with test drug**	**recovered**
0050007	3290	M	white	53 yr	Post Viral Fail Optm	MK-0518	800.00 mg	456	Suicidal ideation	7 day	614	severe	Y	def not	no action with test drug	recovered
0050021	3896	M	white	57 yr	Post Viral Fail Max	MK-0518	1200.00 mg	281	Dyspnoea	3 day	397	severe	Y	prob not	no action with test drug	recovered
						MK-0518	1200.00 mg	281	Fatigue	1 hr	397	mod	Y	prob not	no action with test drug	recovered
	3897	F	white	36 yr	Post Viral Fail Optm	MK-0518	800.00 mg	455	**Pleural effusion**	CONT	564	mod	Y	def not	no action with test drug	not recovered
0050024	3240	M	white	47 yr	Post Viral Fail Optm	MK-0518	800.00 mg	441	Hodgkin's disease	CONT	518	mod	Y	def not	no action with test drug	not recovered
0050030	3292	M	white	57 yr	Post Viral Fail Max	Off Drug 14 days		237	Portal hypertension	3 day	596	severe	Y	prob not	no action with test drug	recovered

Listing of Patients With Serious Clinical Adverse Experiences—Open-Label Post Virologic Failure Phase
(Protocols 005, 018, and 019) - *Cumulative Data*

Study Number	AN	Gen-der	Race	Age	Period	Therapy	Total Daily Dose	Rela-tive Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontin-uance†	Intensity	Ser-ious	Drug Relation-Ship	Action Taken	Outcome
MK-0518																
0050030	**3292**	**M**	**white**	**57 yr**	**Post Viral Fail Optm**	**Off Drug 11 days**		**607**	**Oesophageal varices haemorrhage**	**5 day**	**596**	**severe**	**Y**	**prob not**	**interrupted PRx**	**recovered**
0050033	3281	M	white	52 yr	Post Viral Fail Max	MK-0518	1200.00 mg	211	Hodgkin's disease	CONT	519	severe	Y	prob not	no action with test drug	not recovered
						MK-0518	1200.00 mg	254	Basal cell carcinoma	2 day	519	mod	Y	def not	no action with test drug	recovered
						MK-0518	1200.00 mg	316	Bone marrow toxicity	16 day	519	mod	Y	def not	no action with test drug	recovered
	3285	M	white	43 yr	Post Viral Fail Max	MK-0518	1200.00 mg	334	Pneumonia	7 day	557	severe	Y	def not	no action with test drug	recovered
						MK-0518	1200.00 mg	334	Sepsis	7 day	557	severe	Y	def not	no action with test drug	recovered

Listing of Patients With Serious Clinical Adverse Experiences—Open-Label Post Virologic Failure Phase
(Protocols 005, 018, and 019) - *Cumulative Data*

Study Number	AN	Gender	Race	Age	Period	Therapy	Total Daily Dose	Relative Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontinuance†	Intensity	Serious	Drug Relationship	Action Taken	Outcome
MK-0518																
0180013	7054	M	white	43 yr	OL Post Viral Fail	MK-0518	800.00 mg	180	Varicella	9 day	238	mod	Y	prob not	no action with test drug	recovered
0180017	7083	M	white	51 yr	OL Post Viral Fail	MK-0518	800.00 mg	158	Angina unstable	4 day	248	mod	Y	prob not	no action with test drug	recovered
	8249	F	white	39 yr	OL Post Viral Fail	MK-0518	800.00 mg	140	Cytomegalovirus chorioretinitis	CONT	248	mod	Y	def not	no action with test drug	not recovered
0180018	**8288**	**M**	**white**	**45 yr**	**OL Post Viral Fail**	**MK-0518**	**800.00 mg**	**181**	**Anal cancer**	**19 day**	**238**	**mod**	**Y**	**def not**	**no action with test drug**	**recovered**
0180023	6402	M	white	40 yr	OL Post Viral Fail	MK-0518	800.00 mg	202	Oesophageal candidiasis	CONT	290	mild	Y	def not	no action with test drug	not recovered
0180058	**7005**	**M**	**white**	**60 yr**	**OL Post Viral Fail**	**Off Drug 1 day**		**279**	**Septic shock**	**6 day**	**280**	**severe**	**Y**	**def not**	**discontinued PRx**	**recovered**
0180059	8205	M	white	41 yr	OL Post Viral Fail	MK-0518	1600.00 mg	155	Accidental overdose	1 day	294	mild	Y	def not	no action with test drug	recovered

Listing of Patients With Serious Clinical Adverse Experiences—Open-Label Post Virologic Failure Phase
(Protocols 005, 018, and 019) - *Cumulative Data*

Study Number	AN	Gender	Race	Age	Period	Therapy	Total Daily Dose	Relative Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontinuance†	Intensity	Serious	Drug Relationship	Action Taken	Outcome
MK-0518																
0180062	**8215**	**M**	**white**	**43 yr**	**OL Post Viral Fail**	**MK-0518**	**800.00 mg**	**235**	**Epididymitis**	**CONT**	**300**	**mild**	**Y**	**prob not**	**no action with test drug**	**not recovered**
0190010	**16279**	**M**	**black**	**47 yr**	**OL Post Viral Fail**	**Off Drug 4 days**		**243**	**Pneumocystis jiroveci pneumonia**	**16 day**	**267**	**severe**	**Y**	**def not**	**interrupted PRx**	**recovered**
0190015	16233	M	white	38 yr	OL Post Viral Fail	MK-0518	800.00 mg	129	Immune reconstitution syndrome	7 day	282	mild	Y	Poss	no action with test drug	recovered
0190016	16237	F	black	41 yr	OL Post Viral Fail	MK-0518	800.00 mg	145	Cholecystitis acute	10 day	272	severe	Y	def not	interrupted PRx	recovered
						Off Drug 14 days		166	Failure to thrive	CONT	272	mod	Y	def not	interrupted PRx	not recovered
	16260	F	black	54 yr	OL Post Viral Fail	MK-0518	800.00 mg	184	Arthritis bacterial	CONT	252	mod	Y	def not	no action with test drug	not recovered

Listing of Patients With Serious Clinical Adverse Experiences—Open-Label Post Virologic Failure Phase
(Protocols 005, 018, and 019) - *Cumulative Data*

Study Number	AN	Gender	Race	Age	Period	Therapy	Total Daily Dose	Relative Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontinuance†	Intensity	Serious	Drug Relationship	Action Taken	Outcome
MK-0518																
0190031	**15089**	**M**	**Hispa**	**20 yr**	**OL Post Viral Fail**	**MK-0518**	**800.00 mg**	**150**	**Pneumococcal sepsis**	**4 day**	**204**	**mod**	**Y**	**def not**	**no action with test drug**	**recovered**
						MK-0518	**800.00 mg**	**150**	**Pyrexia**	**4 day**	**204**	**mod**	**Y**	**def not**	**no action with test drug**	**recovered**
	16231	M	black	17 yr	OL Post Viral Fail	MK-0518	800.00 mg	199	Gastroenteritis salmonella	6 day	247	mod	Y	def not	no action with test drug	recovered
						Off Drug 13 days		**260**	**Gastroenteritis**	**5 day**	**247**	**mod**	**Y**	**def not**	**no action with test drug**	**recovered**
	16234	M	black	16 yr	OL Post Viral Fail	MK-0518	800.00 mg	197	Henoch-Schonlein purpura	11 day	259	mod	Y	prob not	interrupted PRx	recovered
	16254	F	black	19 yr	OL Post Viral Fail	MK-0518	800.00 mg	148	Subcutaneous abscess	13 day	187	severe	Y	def not	no action with test drug	recovered
						MK-0518	800.00 mg	170	Staphylococcal abscess	CONT	187	mod	Y	def not	no action with test drug	not recovered

Listing of Patients With Serious Clinical Adverse Experiences—Open-Label Post Virologic Failure Phase
(Protocols 005, 018, and 019) - *Cumulative Data*

Study Number	AN	Gen-der	Race	Age	Period	Therapy	Total Daily Dose	Rela-tive Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontin-uance†	Intensity	Ser-ious	Drug Relation-Ship	Action Taken	Outcome
MK-0518																
0190031	16254	F	black	19 yr	OL Post Viral Fail	MK-0518	800.00 mg	177	Progressive multifocal Leuko-encephalopathy	2.07 mo	187	mild	Y	def not	no action with test drug	fatal
0190053	**15046**	**M**	**white**	**49 yr**	**OL Post Viral Fail**	**Off Drug 3 days**		**239**	**Depression**	**1.87 mo**	**236**	**severe**	**Y**	**Poss**	**no action with test drug**	**recovered**
	16267	**M**	**white**	**46 yr**	**OL Post Viral Fail**	**Off Drug 8 days**		**245**	**Diarrhoea**	**CONT**	**237**	**severe**	**Y**	**Poss**	**no action with test drug**	**not recovered**
0190054	15014	M	white	41 yr	OL Post Viral Fail	MK-0518	800.00 mg	183	Cytomegalovirus chorioretinitis	10 day	293	severe	Y	def not	interrupted PRx	recovered

†Day study therapy was discontinued relative to the start of study therapy.
Note: MK-0518 and Placebo were administered with Optimized Background Therapy (OBT).
Adverse experience terms are from MedDRA Version 9.1.
Drug Relationship: def = definitely, def not = definitely not, poss = possibly, prob = probably, prob not = probably not.
Intensity: mod = moderate.

[Ref. 5.3.5.1: P005-Define, P018-Define, P019-Define]

Appendix 2.7.4: 54

Number (%) of Patients With Specific Clinical Adverse Experiences of Rash and Related Terms (Incidence >0% in One or More Treatment Groups) by System Organ Class – Patients in the Treatment Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Cumulative Data*

	MK-0518 400 mg b.i.d. (N = 507)		Placebo (N = 282)		Total (N = 789)	
	n	(%)	n	(%)	n	(%)
Patients With One Or More Adverse Experiences	40	(7.9)	11	(3.9)	51	(6.5)
Patients With No Adverse Experience	467	(92.1)	271	(96.1)	738	(93.5)
Skin And Subcutaneous Tissue Disorders	40	(7.9)	11	(3.9)	51	(6.5)
Rash	27	(5.3)	7	(2.5)	34	(4.3)
Rash Follicular	1	(0.2)	0	(0.0)	1	(0.1)
Rash Generalised	1	(0.2)	0	(0.0)	1	(0.1)
Rash Macular	3	(0.6)	1	(0.4)	4	(0.5)
Rash Maculo-Papular	4	(0.8)	1	(0.4)	5	(0.6)
Rash Papular	3	(0.6)	2	(0.7)	5	(0.6)
Rash Pruritic	2	(0.4)	0	(0.0)	2	(0.3)

Although a patient may have had two or more clinical adverse experiences, the patient is counted only once within a category. The same patient may appear in different categories.

Note: MK-0518 and Placebo were administered with Optimized Background Therapy (OBT).

Adverse experience terms are from MedDRA Version 9.1.

[Ref. 5.3.5.1: P005-Define, P018-Define, P019-Define]

Appendix 2.7.4: 55

Number (%) of Patients With Specific Clinical Adverse Experiences of Rash and Related Terms (Incidence >0% in One or More Treatment Groups) by System Organ Class – Patients in the Treatment Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Original Application*

	MK-0518 400 mg b.i.d. (N = 507)		Placebo (N = 282)		Total (N = 789)	
	n	(%)	n	(%)	n	(%)
Patients With One Or More Adverse Experiences	34	(6.7)	11	(3.9)	45	(5.7)
Patients With No Adverse Experience	473	(93.3)	271	(96.1)	744	(94.3)
Skin And Subcutaneous Tissue Disorders	34	(6.7)	11	(3.9)	45	(5.7)
Rash	23	(4.5)	8	(2.8)	31	(3.9)
Rash Follicular	1	(0.2)	0	(0.0)	1	(0.1)
Rash Generalised	1	(0.2)	0	(0.0)	1	(0.1)
Rash Macular	2	(0.4)	1	(0.4)	3	(0.4)
Rash Maculo-Papular	2	(0.4)	1	(0.4)	3	(0.4)
Rash Papular	4	(0.8)	1	(0.4)	5	(0.6)
Rash Pruritic	2	(0.4)	0	(0.0)	2	(0.3)

Although a patient may have had two or more clinical adverse experiences, the patient is counted only once within a category. The same patient may appear in different categories.

Note: MK-0518 and Placebo were administered with Optimized Background Therapy (OBT).

Adverse experience terms are from MedDRA Version 9.1.

[Ref. 5.3.5.1: P005, P018, P019]

Appendix 2.7.4: 56

Number (%) of Patients With Specific Drug-Related Clinical Adverse Experiences of Rash and Related Terms (Incidence >0% in One or More Treatment Groups) by System Organ Class—Related to MK-0518 or Placebo (Alone or in Combination With Optimized Background Therapy)—Treatment-Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Cumulative Data*

	MK-0518 400 mg b.i.d. (N = 507)		Placebo (N = 282)		Total (N = 789)	
	n	(%)	n	(%)	n	(%)
Patients With One Or More Adverse Experiences	11	(2.2)	7	(2.5)	18	(2.3)
Patients With No Adverse Experience	496	(97.8)	275	(97.5)	771	(97.7)
Skin And Subcutaneous Tissue Disorders	11	(2.2)	7	(2.5)	18	(2.3)
Rash	7	(1.4)	5	(1.8)	12	(1.5)
Rash Macular	1	(0.2)	1	(0.4)	2	(0.3)
Rash Maculo-Papular	3	(0.6)	1	(0.4)	4	(0.5)

Although a patient may have had two or more clinical adverse experiences, the patient is counted only once within a category. The same patient may appear in different categories.

Note: MK-0518 and Placebo were administered with Optimized Background Therapy (OBT).

Adverse experience terms are from MedDRA Version 9.1.

[Ref. 5.3.5.1: P005-Define, P018-Define, P019-Define]

Appendix 2.7.4: 57

Number (%) of Patients With Specific Drug-Related Clinical Adverse Experiences of Rash and Related Terms (Incidence >0% in One or More Treatment Groups) by System Organ Class—Related to MK-0518 or Placebo (Alone or in Combination With Optimized Background Therapy)—Treatment-Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Original Application*

	MK-0518 400 mg b.i.d. (N = 507)		Placebo (N = 282)		Total (N = 789)	
	n	(%)	n	(%)	n	(%)
Patients With One Or More Adverse Experiences	10	(2.0)	7	(2.5)	17	(2.2)
Patients With No Adverse Experience	497	(98.0)	275	(97.5)	772	(97.8)
Skin And Subcutaneous Tissue Disorders	10	(2.0)	7	(2.5)	17	(2.2)
Rash	6	(1.2)	5	(1.8)	11	(1.4)
Rash Macular	1	(0.2)	1	(0.4)	2	(0.3)
Rash Maculo-Papular	2	(0.4)	1	(0.4)	3	(0.4)
Rash Papular	1	(0.2)	0	(0.0)	1	(0.1)

Although a patient may have had two or more clinical adverse experiences, the patient is counted only once within a category. The same patient may appear in different categories.

Note: MK-0518 and Placebo were administered with Optimized Background Therapy (OBT).

Adverse experience terms are from MedDRA Version 9.1.

[Ref. 5.3.5.1: P005, P018, P019]

Appendix 2.7.4: 58

Listing of Patients With Specific Clinical Adverse Experiences of Rash and Related Terms—Patients in the Treatment Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Cumulative Data*

Study Number	AN	Gender	Race	Age	Period	Therapy	Total Daily Dose	Relative Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontinuance[†]	Intensity	Serious	Drug Relationship	Action Taken	Outcome
MK-0518 400 mg b.i.d.																
0050015	3256	M	white	38 yr	Dose-Ranging	MK-0518	800.00 mg	231	Rash papular	1.97 mo	541	mild	N	prob not	no action with test drug	recovered
						MK-0518	800.00 mg	290	Rash follicular	CONT	541	mild	N	prob not	no action with test drug	not recovered
Placebo																
0050021	3241	F	white	41 yr	Dose-Ranging	Placebo	0.00 mg	161	Rash macular	CONT	525	mod	N	poss	no action with test drug	not recovered
0050024	3591	M	white	29 yr	Dose-Ranging	Placebo	0.00 mg	12	Rash	24 day	443	mild	N	prob not	no action with test drug	recovered
MK-0518 400 mg b.i.d.																
0180004	7118	M	white	54 yr	Double-Blind	MK-0518	800.00 mg	11	Rash	4 day	170	mild	N	prob not	no action with test drug	recovered

Listing of Patients With Specific Clinical Adverse Experiences of Rash and Related Terms—Patients in the Treatment Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Cumulative Data*

Study Number	AN	Gender	Race	Age	Period	Therapy	Total Daily Dose	Relative Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontinuance†	Intensity	Serious	Drug Relationship	Action Taken	Outcome
MK-0518 400 mg b.i.d.																
0180007	7077	M	white	42 yr	Double-Blind	MK-0518	800.00 mg	27	Rash	1.15 mo	230	mild	N	prob not	no action with test drug	recovered
0180008	7053	M	white	58 yr	Double-Blind	MK-0518	800.00 mg	12	Rash	7 day	221	mod	N	prob not	interrupted PRx	recovered
						MK-0518	**800.00 mg**	**200**	**Rash**	**8 day**	**221**	**mild**	**N**	**prob not**	**no action with test drug**	**recovered**
0180010	7073	M	white	62 yr	Double-Blind	MK-0518	800.00 mg	15	Rash maculo-papular	7 day	224	mod	N	poss	no action with test drug	recovered
0180013	7058	M	white	43 yr	Double-Blind	MK-0518	800.00 mg	1	Rash	3 day	226	mod	N	def	no action with test drug	recovered
0180017	8262	M	white	43 yr	Double-Blind	MK-0518	800.00 mg	82	Rash	4 day	234	mod	N	poss	no action with test drug	recovered
0180024	7010	M	white	50 yr	Double-Blind	MK-0518	800.00 mg	86	Rash	1.25 mo	297	mod	N	prob not	no action with test drug	recovered
0180027	8372	M	white	49 yr	Double-Blind	MK-0518	800.00 mg	63	Rash	1.18 mo	189	mild	N	poss	no action with test drug	recovered

Listing of Patients With Specific Clinical Adverse Experiences of Rash and Related Terms—Patients in the Treatment Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Cumulative Data*

Study Number	AN	Gender	Race	Age	Period	Therapy	Total Daily Dose	Relative Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontinuance†	Intensity	Serious	Drug Relationship	Action Taken	Outcome
MK-0518 400 mg b.i.d.																
0180027	**8372**	**M**	**white**	**49 yr**	**Double-Blind**	**MK-0518**	**800.00 mg**	**151**	**Rash**	**CONT**	**189**	**mild**	**N**	**prob not**	**no action with test drug**	**not recovered**
0180030	7030	M	white	49 yr	Double-Blind	MK-0518	800.00 mg	179	Rash	19 day	281	mod	N	prob not	**interrupted PRx**	recovered
0180032	8325	F	black	40 yr	Double-Blind	MK-0518	800.00 mg	26	Rash	18 day	108	mild	N	def not	no action with test drug	recovered
0180041	7033	M	white	62 yr	Double-Blind	MK-0518	800.00 mg	3	Rash	2.69 mo	278	mild	N	prob not	no action with test drug	recovered
0180042	7061	M	white	61 yr	Double-Blind	MK-0518	800.00 mg	28	Rash	1.87 mo	225	mod	N	prob not	no action with test drug	recovered
0180044	7036	M	white	53 yr	Double-Blind	MK-0518	800.00 mg	89	Rash pruritic	5 day	279	mild	N	prob not	no action with test drug	recovered
0180060	7013	M	white	37 yr	Double-Blind	MK-0518	800.00 mg	30	**Rash maculo-papular**	1.45 mo	279	mild	N	poss	no action with test drug	recovered
0180064	7071	M	white	43 yr	Double-Blind	MK-0518	800.00 mg	48	Rash	12 day	224	mild	N	def not	no action with test drug	recovered

Listing of Patients With Specific Clinical Adverse Experiences of Rash and Related Terms—Patients in the Treatment Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Cumulative Data*

Study Number	AN	Gender	Race	Age	Period	Therapy	Total Daily Dose	Relative Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontinuance†	Intensity	Serious	Drug Relationship	Action Taken	Outcome
Placebo																
0180005	**8356**	**M**	**white**	**46 yr**	**Double-Blind**	**Placebo**	**0.00 mg**	**16**	**Rash**	**9 day**	**219**	**mild**	**N**	**poss**	**no action with test drug**	**recovered**
						Placebo	0.00 mg	42	Rash	13 day	219	mild	N	def not	no action with test drug	recovered
0180010	8378	M	white	43 yr	Double-Blind	Placebo	0.00 mg	13	Rash maculopapular	25 day	168	mod	N	poss	no action with test drug	recovered
0180034	8301	M	multi	33 yr	Double-Blind	Placebo	0.00 mg	4	Rash	1.48 mo	246	mild	N	poss	no action with test drug	recovered
0180036	8339	F	multi	35 yr	Double-Blind	Placebo	0.00 mg	10	Rash	1 day	224	mild	N	def not	no action with test drug	recovered
MK-0518 400 mg b.i.d.																
0190005	16211	M	Hispa	39 yr	Double-Blind	MK-0518	800.00 mg	156	Rash	2.66 mo	281	mild	N	def not	no action with test drug	recovered

Listing of Patients With Specific Clinical Adverse Experiences of Rash and Related Terms—Patients in the Treatment Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Cumulative Data*

Study Number	AN	Gender	Race	Age	Period	Therapy	Total Daily Dose	Relative Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontinuance†	Intensity	Serious	Drug Relationship	Action Taken	Outcome
MK-0518 400 mg b.i.d.																
0190010	15057	M	white	48 yr	Double-Blind	MK-0518	800.00 mg	107	Rash generalised	9 day	230	mod	N	def not	no action with test drug	recovered
	16276	M	black	21 yr	Double-Blind	MK-0518	800.00 mg	12	Rash	1.22 mo	227	mod	N	def not	no action with test drug	recovered
0190011	16322	M	white	39 yr	Double-Blind	MK-0518	800.00 mg	16	Rash maculo-papular	5.42 mo	224	mild	N	poss	no action with test drug	recovered
0190013	16278	M	Hispa	44 yr	Double-Blind	MK-0518	800.00 mg	148	Rash	3 day	227	mod	N	def not	no action with test drug	recovered
0190014	16247	M	white	45 yr	Double-Blind	MK-0518	800.00 mg	3	Rash papular	12 day	261	mild	N	prob not	no action with test drug	recovered
						MK-0518	800.00 mg	22	Rash papular	2.30 mo	261	mild	N	prob not	no action with test drug	recovered
0190015	16232	M	black	44 yr	Double-Blind	MK-0518	800.00 mg	144	Rash pruritic	CONT	275	mild	N	prob not	no action with test drug	not recovered

Listing of Patients With Specific Clinical Adverse Experiences of Rash and Related Terms—Patients in the Treatment Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Cumulative Data*

Study Number	AN	Gender	Race	Age	Period	Therapy	Total Daily Dose	Relative Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontinuance†	Intensity	Serious	Drug Relationship	Action Taken	Outcome
MK-0518 400 mg b.i.d.																
0190016	15603	M	black	39 yr	Double-Blind	MK-0518	800.00 mg	42	Rash papular	CONT	280	mild	N	def not	no action with test drug	not recovered
0190021	**15055**	**M**	**white**	**43 yr**	**Double-Blind**	**Off Drug 1 day**		**232**	**Rash macular**	**CONT**	**231**	**mild**	**N**	**prob not**	**no action with test drug**	**not recovered**
	15065	**M**	**white**	**40 yr**	**Double-Blind**	**Off Drug 2 days**		**229**	**Rash**	**CONT**	**227**	**mild**	**N**	**def not**	**no action with test drug**	**not recovered**
0190023	**16257**	**M**	**white**	**43 yr**	**Double-Blind**	**MK-0518**	**800.00 mg**	**205**	**Rash**	**10 day**	**280**	**mild**	**N**	**def not**	**no action with test drug**	**recovered**
0190027	**16365**	**M**	**black**	**48 yr**	**Double-Blind**	**MK-0518**	**800.00 mg**	**27**	**Rash**	**29 day**	**164**	**mild**	**N**	**prob not**	**no action with test drug**	**recovered**
	16409	**M**	**black**	**43 yr**	**Double-Blind**	**MK-0518**	**800.00 mg**	**54**	**Rash**	**1.97 mo**	**168**	**mild**	**N**	**poss**	**no action with test drug**	**recovered**
0190032	15005	M	white	46 yr	Double-Blind	MK-0518	800.00 mg	41	Rash	1.41 mo	315	mod	N	poss	no action with test drug	recovered

Listing of Patients With Specific Clinical Adverse Experiences of Rash and Related Terms—Patients in the Treatment Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Cumulative Data*

Study Number	AN	Gender	Race	Age	Period	Therapy	Total Daily Dose	Relative Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontinuance†	Intensity	Serious	Drug Relationship	Action Taken	Outcome
MK-0518 400 mg b.i.d.																
0190035	16353	M	white	22 yr	Double-Blind	MK-0518	800.00 mg	9	Rash macular	9 day	169	mod	N	prob	no action with test drug	recovered
0190037	16302	M	Hispa	33 yr	Double-Blind	MK-0518	800.00 mg	10	Rash	15 day	239	severe	N	prob not	no action with test drug	recovered
0190044	16272	M	white	49 yr	Double-Blind	MK-0518	800.00 mg	8	Rash	3 day	231	mild	N	prob	no action with test drug	recovered
0190045	16291	M	white	56 yr	Double-Blind	MK-0518	800.00 mg	8	Rash	21 day	223	mod	N	prob	no action with test drug	recovered
	16318	M	white	50 yr	Double-Blind	MK-0518	800.00 mg	11	Rash macular	6.28 mo	200	mild	N	def not	no action with test drug	recovered
0190047	15119	M	Hispa	54 yr	Double-Blind	MK-0518	800.00 mg	55	Rash	1.05 mo	168	mod	N	def not	no action with test drug	recovered
						MK-0518	800.00 mg	86	Rash	30 day	168	mild	N	def not	no action with test drug	recovered

Listing of Patients With Specific Clinical Adverse Experiences of Rash and Related Terms—Patients in the Treatment Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Cumulative Data*

Study Number	AN	Gender	Race	Age	Period	Therapy	Total Daily Dose	Relative Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontinuance†	Intensity	Serious	Drug Relationship	Action Taken	Outcome
MK-0518 400 mg b.i.d.																
0190048	15029	M	white	52 yr	Double-Blind	MK-0518	800.00 mg	2	Rash	9.43 mo	224	mild	N	def not	no action with test drug	recovered
0190051	**15012**	**M**	**white**	**59 yr**	**Double-Blind**	**MK-0518**	**800.00 mg**	**251**	**Rash maculo-papular**	**CONT**	**280**	**mild**	**N**	**prob not**	**no action with test drug**	**not recovered**
	15040	M	white	51 yr	Double-Blind	MK-0518	800.00 mg	108	Rash	15 day	278	mild	N	def not	no action with test drug	recovered
0190054	16363	M	white	59 yr	Double-Blind	MK-0518	800.00 mg	79	Rash	2.92 mo	172	mild	N	def not	no action with test drug	recovered
Placebo																
0190024	15002	M	black	59 yr	Double-Blind	Placebo	0.00 mg	49	Rash	8 day	300	mod	N	poss	no action with test drug	recovered
0190027	**15114**	**M**	**black**	**40 yr**	**Double-Blind**	**Placebo**	**0.00 mg**	**84**	**Rash papular**	**28 day**	**168**	**mild**	**N**	**prob not**	**no action with test drug**	**recovered**

Listing of Patients With Specific Clinical Adverse Experiences of Rash and Related Terms—Patients in the Treatment Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Cumulative Data*

Study Number	AN	Gender	Race	Age	Period	Therapy	Total Daily Dose	Relative Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontinuance†	Intensity	Serious	Drug Relationship	Action Taken	Outcome
Placebo																
0190032	16399	F	black	41 yr	Double-Blind	Placebo	0.00 mg	80	Rash papular	2.20 mo	170	mild	N	def not	no action with test drug	recovered
0190034	16389	M	multi	49 yr	Double-Blind	Placebo	0.00 mg	4	Rash	10 day	167	mild	N	poss	interrupted PRx	recovered
0190035	16355	M	white	52 yr	Double-Blind	Placebo	0.00 mg	11	Rash	11 day	188	mod	N	prob	no action with test drug	recovered

†Day study therapy was discontinued relative to the start of study therapy.

Drug Relationship: def = definitely, def not = definitely not, poss = possibly, prob = probably, prob not = probably not

Intensity: mod = moderate

Note: MK-0518 and Placebo were administered with Optimized Background Therapy (OBT).

Adverse experience terms are from MedDRA Version 9.1.

[Ref. 5.3.5.1: P005-Define, P018-Define, P019-Define]

Appendix 2.7.4: 59

Listing of Patients With Specific Drug-Related Clinical Adverse Experiences of Rash and Related Terms—Related to MK-0518 or Placebo (Alone or in Combination With Optimized Background Therapy)—Patients in the Treatment Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Cumulative Data*

Study Number	AN	Gender	Race	Age	Period	Therapy	Total Daily Dose	Relative Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontinuance†	Intensity	Serious	Drug Relationship	Action Taken	Outcome
Placebo																
0050021	3241	F	white	41 yr	Dose-Ranging	Placebo	0.00 mg	161	Rash macular	CONT	525	mod	N	poss	no action with test drug	not recovered
MK-0518 400 mg b.i.d.																
0180010	7073	M	white	62 yr	Double-Blind	MK-0518	800.00 mg	15	Rash maculo-papular	7 day	224	mod	N	poss	no action with test drug	recovered
0180013	7058	M	white	43 yr	Double-Blind	MK-0518	800.00 mg	1	Rash	3 day	226	mod	N	def	no action with test drug	recovered
0180017	8262	M	white	43 yr	Double-Blind	MK-0518	800.00 mg	82	Rash	4 day	234	mod	N	poss	no action with test drug	recovered
0180027	8372	M	white	49 yr	Double-Blind	MK-0518	800.00 mg	63	Rash	1.18 mo	189	mild	N	poss	no action with test drug	recovered
0180060	7013	M	white	37 yr	Double-Blind	MK-0518	800.00 mg	30	**Rash maculo-papular**	1.45 mo	279	mild	N	poss	no action with test drug	recovered

Listing of Patients With Specific Drug-Related Clinical Adverse Experiences of Rash and Related Terms—Related to MK-0518 or Placebo (Alone or in Combination With Optimized Background Therapy)—Patients in the Treatment Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Cumulative Data*

Study Number	AN	Gender	Race	Age	Period	Therapy	Total Daily Dose	Relative Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontinuance†	Intensity	Serious	Drug Relationship	Action Taken	Outcome
Placebo																
0180005	8356	M	white	46 yr	Double-Blind	Placebo	0.00 mg	16	Rash	9 day	219	mild	N	poss	no action with test drug	recovered
0180010	8378	M	white	43 yr	Double-Blind	Placebo	0.00 mg	13	Rash maculo-papular	25 day	168	mod	N	poss	no action with test drug	recovered
0180034	8301	M	multi	33 yr	Double-Blind	Placebo	0.00 mg	4	Rash	1.48 mo	246	mild	N	poss	no action with test drug	recovered
MK-0518 400 mg b.i.d.																
0190011	16322	M	white	39 yr	Double-Blind	MK-0518	800.00 mg	16	Rash maculo-papular	5.42 mo	224	mild	N	poss	no action with test drug	recovered
0190027	**16409**	**M**	**black**	**43 yr**	**Double-Blind**	**MK-0518**	**800.00 mg**	**54**	**Rash**	**1.97 mo**	**168**	**mild**	**N**	**poss**	**no action with test drug**	**recovered**
0190032	15005	M	white	46 yr	Double-Blind	MK-0518	800.00 mg	41	Rash	1.41 mo	315	mod	N	poss	no action with test drug	recovered

Listing of Patients With Specific Drug-Related Clinical Adverse Experiences of Rash and Related Terms—Related to MK-0518 or Placebo (Alone or in Combination With Optimized Background Therapy)—Patients in the Treatment Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Cumulative Data*

Study Number	AN	Gender	Race	Age	Period	Therapy	Total Daily Dose	Relative Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontinuance†	Intensity	Serious	Drug Relationship	Action Taken	Outcome
MK-0518 400 mg b.i.d.																
0190035	16353	M	white	22 yr	Double-Blind	MK-0518	800.00 mg	9	Rash macular	9 day	169	mod	N	prob	no action with test drug	recovered
0190044	16272	M	white	49 yr	Double-Blind	MK-0518	800.00 mg	8	Rash	3 day	231	mild	N	prob	no action with test drug	recovered
0190045	16291	M	white	56 yr	Double-Blind	MK-0518	800.00 mg	8	Rash	21 day	223	mod	N	prob	no action with test drug	recovered
Placebo																
0190024	15002	M	black	59 yr	Double-Blind	Placebo	0.00 mg	49	Rash	8 day	300	mod	N	poss	no action with test drug	recovered

Listing of Patients With Specific Drug-Related Clinical Adverse Experiences of Rash and Related Terms—Related to MK-0518 or Placebo (Alone or in Combination With Optimized Background Therapy)—Patients in the Treatment Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Cumulative Data*

Study Number	AN	Gender	Race	Age	Period	Therapy	Total Daily Dose	Relative Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontinuance[†]	Intensity	Serious	Drug Relationship	Action Taken	Outcome
Placebo																
0190034	16389	M	multi	49 yr	Double-Blind	Placebo	0.00 mg	4	Rash	10 day	167	mild	N	poss prob	interrupted PRx no action with test drug	recovered
0190035	16355	M	white	52 yr	Double-Blind	Placebo	0.00 mg	11	Rash	11 day	188	mod	N			recovered

[†]Day study therapy was discontinued relative to the start of study therapy.

Drug Relationship: def = definitely, def not = definitely not, poss = possibly, prob = probably, prob not = probably not

Intensity: mod = moderate

Note: MK-0518 and Placebo were administered with Optimized Background Therapy (OBT).

Adverse experience terms are from MedDRA Version 9.1.

[Ref. 5.3.5.1: P005-Define, P018-Define, P019-Define]

Appendix 2.7.4: 60

Number (%) of Patients With Specific Clinical Adverse Experiences of Rash and Related Terms (Incidence >0% in One or More Treatment Groups) by System Organ Class—Open-Label Post Virologic Failure Phase (Protocols 005, 018, and 019) - *Cumulative Data*

	MK-0518 (N = 223)	
	n	(%)
Patients With One Or More Adverse Experiences	13	(5.8)
Patients With No Adverse Experience	210	(94.2)
Skin And Subcutaneous Tissue Disorders	13	(5.8)
Rash	10	(4.5)
Rash Maculo-Papular	1	(0.4)
Rash Papular	2	(0.9)
Rash Pruritic	1	(0.4)

Although a patient may have had two or more clinical adverse experiences, the patient is counted only once within a category. The same patient may appear in different categories.

Note: MK-0518 and Placebo were administered with Optimized Background Therapy (OBT).

Adverse experience terms are from MedDRA Version 9.1.

[Ref. 5.3.5.1: P005-Define, P018-Define, P019-Define]

Appendix 2.7.4: 61

Number (%) of Patients With Specific Clinical Adverse Experiences of Rash and Related Terms (Incidence >0% in One or More Treatment Groups) by System Organ Class—Open-Label Post Virologic Failure Phase (Protocols 005, 018, and 019) - *Original Application*

	MK-0518 (N = 177)	
	n	(%)
Patients With One Or More Adverse Experiences	7	(4.0)
Patients With No Adverse Experience	170	(96.0)
Skin And Subcutaneous Tissue Disorders	7	(4.0)
Rash	5	(2.8)
Rash Macular	1	(0.6)
Rash Maculo-Papular	1	(0.6)
Rash Pruritic	1	(0.6)

Although a patient may have had two or more clinical adverse experiences, the patient is counted only once within a category. The same patient may appear in different categories.

Note: MK-0518 and Placebo were administered with Optimized Background Therapy (OBT).

Adverse experience terms are from MedDRA Version 9.1.

[Ref. 5.3.5.1: P005, P018, P019]

Appendix 2.7.4: 62

Listing of Patients With Specific Clinical Adverse Experiences of Rash and Related Terms– Open-Label Post Virologic Failure Phase (Protocols 005, 018, and 019) - *Cumulative Data*

Study Number	AN	Gen-der	Race	Age	Period	Therapy	Total Daily Dose	Rela-tive Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontin-uance†	Intensity	Ser-ious	Drug Relation-ship	Action Taken	Outcome
MK-0518																
0050002	3595	M	white	44 yr	Post Viral Fail Optm	MK-0518	400.00 mg	260	Rash papular	13 day	463	mild	N	poss	no action with test drug	recovered
0050032	3287	M	white	57 yr	Post Viral Fail Max	MK-0518	1200.00 mg	185	Rash	CONT	268	mild	N	poss	no action with test drug	not recovered
					Post-Treatment PVFM	Off Drug 13 days		281	Rash maculo-papular	6 day	268	mod	N	def not	no action with test drug	recovered
MK-0518																
0180003	8280	M	Asian	36 yr	OL Post Viral Fail	MK-0518	800.00 mg	195	Rash pruritic	29 day	251	mild	N	prob not	no action with test drug	recovered
0180034	**8301**	**M**	**multi**	**33 yr**	**OL Post Viral Fail**	**MK-0518**	**800.00 mg**	**182**	**Rash**	**5 day**	**246**	**mild**	**N**	**poss**	**no action with test drug**	**recovered**
						MK-0518	**800.00 mg**	**205**	**Rash**	**CONT**	**246**	**mod**	**N**	**poss**	**no action with test drug**	**not recovered**

Listing of Patients With Specific Clinical Adverse Experiences of Rash and Related Terms– Open-Label Post Virologic Failure Phase (Protocols 005, 018, and 019) - *Cumulative Data*

Study Number	AN	Gen-der	Race	Age	Period	Therapy	Total Daily Dose	Rela-tive Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontin-uance†	Intensity	Ser-ious	Drug Relation-ship	Action Taken	Outcome
MK-0518																
0180042	7025	M	white	41 yr	OL Post Viral Fail	MK-0518	800.00 mg	202	Rash	1.91 mo	279	mild	N	prob not	no action with test drug	recovered
						MK-0518	**800.00 mg**	**223**	**Rash**	**1.22 mo**	**279**	**mod**	**N**	**prob not**	**no action with test drug**	**recovered**
0180051	**7120**	**M**	**white**	**52 yr**	**OL Post Viral Fail**	**MK-0518**	**800.00 mg**	**172**	**Rash**	**1.38 mo**	**183**	**mild**	**N**	**poss**	**no action with test drug**	**recovered**
	8299	**M**	**white**	**43 yr**	**OL Post Viral Fail**	**MK-0518**	**800.00 mg**	**187**	**Rash**	**10 day**	**246**	**mild**	**N**	**prob not**	**no action with test drug**	**recovered**
0180063	8235	M	white	43 yr	OL Post Viral Fail	MK-0518	800.00 mg	163	Rash	1.48 mo	266	mod	N	def not	no action with test drug	recovered
MK-0518																
0190009	**15019**	**M**	**white**	**42 yr**	**OL Post Viral Fail**	**MK-0518**	**800.00 mg**	**245**	**Rash**	**12 day**	**287**	**mild**	**N**	**poss**	**no action with test drug**	**recovered**
0190014	**16247**	**M**	**white**	**45 yr**	**OL Post Viral Fail**	**MK-0518**	**800.00 mg**	**157**	**Rash papular**	**1.08 mo**	**261**	**mild**	**N**	**prob not**	**no action with test drug**	**recovered**

Listing of Patients With Specific Clinical Adverse Experiences of Rash and Related Terms– Open-Label Post Virologic Failure Phase (Protocols 005, 018, and 019) - *Cumulative Data*

Study Number	AN	Gender	Race	Age	Period	Therapy	Total Daily Dose	Relative Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontinuance†	Intensity	Serious	Drug Relationship	Action Taken	Outcome
MK-0518																
0190024	15002	M	black	59 yr	OL Post Viral Fail	MK-0518	800.00 mg	189	Rash	CONT	300	mild	N	def not	no action with test drug	not recovered
0190031	**16234**	**M**	**black**	**16 yr**	**OL Post Viral Fail**	**MK-0518**	**800.00 mg**	**193**	**Rash**	**15 day**	**259**	**mod**	**N**	**prob not**	**no action with test drug**	**recovered**
0190032	**16399**	**F**	**black**	**41 yr**	**OL Post Viral Fail**	**MK-0518**	**800.00 mg**	**127**	**Rash**	**4 day**	**170**	**mod**	**N**	**def**	**interrupted PRx**	**recovered**

†Day study therapy was discontinued relative to the start of study therapy.
Drug Relationship: def = definitely, def not = definitely not, poss = possibly, prob = probably, prob not = probably not
Intensity: mod = moderate
Note: MK-0518 and Placebo were administered with Optimized Background Therapy (OBT).
Adverse experience terms are from MedDRA Version 9.1.

[Ref. 5.3.5.1: P005-Define, P018-Define, P019-Define]

Appendix 2.7.4: 63

Number (%) of Patients With Specific Clinical Adverse Experiences of Rash and Related Terms (Incidence >0% in One or More Treatment Groups) by System Organ Class–Patients Who Received OBT With Darunavir in the Treatment Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Cumulative Data*

	MK-0518 400 mg b.i.d. (N = 193)		Placebo (N = 101)		Total (N = 294)	
	n	(%)	n	(%)	n	(%)
Patients With One Or More Adverse Experiences	26	(13.5)	4	(4.0)	30	(10.2)
Patients With No Adverse Experience	167	(86.5)	97	(96.0)	264	(89.8)
Skin And Subcutaneous Tissue Disorders	26	(13.5)	4	(4.0)	30	(10.2)
Rash	18	(9.3)	1	(1.0)	19	(6.5)
Rash Generalised	1	(0.5)	0	(0.0)	1	(0.3)
Rash Macular	2	(1.0)	0	(0.0)	2	(0.7)
Rash Maculo-Papular	4	(2.1)	1	(1.0)	5	(1.7)
Rash Papular	0	(0.0)	2	(2.0)	2	(0.7)
Rash Pruritic	1	(0.5)	0	(0.0)	1	(0.3)

Although a patient may have had two or more clinical adverse experiences, the patient is counted only once within a category. The same patient may appear in different categories.

Note: MK-0518 and Placebo were administered with Optimized Background Therapy (OBT).

Adverse experience terms are from MedDRA Version 9.1.

[Ref. 5.3.5.1: P005-Define, P018-Define, P019-Define]

Appendix 2.7.4: 64

Number (%) of Patients With Specific Clinical Adverse Experiences of Rash and Related Terms (Incidence >0% in One or More Treatment Groups) by System Organ Class–Patients Who Received OBT With Darunavir in the Treatment Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Original Application*

	MK-0518 400 mg b.i.d. (N = 192)		Placebo (N = 101)		Total (N = 293)	
	n	(%)	n	(%)	n	(%)
Patients With One Or More Adverse Experiences	20	(10.4)	4	(4.0)	24	(8.2)
Patients With No Adverse Experience	172	(89.6)	97	(96.0)	269	(91.8)
Skin And Subcutaneous Tissue Disorders	20	(10.4)	4	(4.0)	24	(8.2)
Rash	14	(7.3)	2	(2.0)	16	(5.5)
Rash Generalised	1	(0.5)	0	(0.0)	1	(0.3)
Rash Macular	1	(0.5)	0	(0.0)	1	(0.3)
Rash Maculo-Papular	2	(1.0)	1	(1.0)	3	(1.0)
Rash Papular	1	(0.5)	1	(1.0)	2	(0.7)
Rash Pruritic	1	(0.5)	0	(0.0)	1	(0.3)

Although a patient may have had two or more clinical adverse experiences, the patient is counted only once within a category. The same patient may appear in different categories.

Note: MK-0518 and Placebo were administered with Optimized Background Therapy (OBT).

Adverse experience terms are from MedDRA Version 9.1.

[Ref. 5.3.5.1: P005, P018, P019]

Appendix 2.7.4: 65

Listing of Patients With Specific Clinical Adverse Experiences of Rash and Related Terms
(Incidence >0% in One or More Treatment Groups) by System Organ Class–Patients Who Received OBT With Darunavir in the Treatment Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Cumulative Data*

Study Number	AN	Gen-der	Race	Age	Period	Therapy	Total Daily Dose	Rela-tive Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontin-uance†	Intensity	Ser-ious	Drug Relation-ship	Action Taken	Outcome
MK-0518 400 mg b.i.d.																
0180007	7077	M	white	42 yr	Double-Blind	MK-0518	800.00 mg	27	Rash	1.15 mo	230	mild	N	prob not	no action with test drug	recovered
0180008	7053	M	white	58 yr	Double-Blind	MK-0518	800.00 mg	12	Rash	7 day	221	mod	N	prob not	interrupted PRx	recovered
						MK-0518	**800.00 mg**	**200**	**Rash**	**8 day**	**221**	**mild**	**N**	**prob not**	**no action with test drug**	**recovered**
0180010	7073	M	white	62 yr	Double-Blind	MK-0518	800.00 mg	15	Rash maculo-papular	7 day	224	mod	N	poss	no action with test drug	recovered
0180030	7030	M	white	49 yr	Double-Blind	MK-0518	800.00 mg	179	Rash	19 day	281	mod	N	prob not	**interrupted PRx**	recovered
0180032	8325	F	black	40 yr	Double-Blind	MK-0518	800.00 mg	26	Rash	18 day	108	mild	N	def not	no action with test drug	recovered
0180041	7033	M	white	62 yr	Double-Blind	MK-0518	800.00 mg	3	Rash	2.69 mo	278	mild	N	prob not	no action with test drug	recovered
0180042	7061	M	white	61 yr	Double-Blind	MK-0518	800.00 mg	28	Rash	1.87 mo	225	mod	N	prob not	no action with test drug	recovered

Listing of Patients With Specific Clinical Adverse Experiences of Rash and Related Terms
(Incidence >0% in One or More Treatment Groups) by System Organ Class–Patients Who Received OBT With Darunavir in the Treatment Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Cumulative Data*

Study Number	AN	Gender	Race	Age	Period	Therapy	Total Daily Dose	Relative Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontinuance†	Intensity	Serious	Drug Relationship	Action Taken	Outcome
MK-0518 400 mg b.i.d.																
0180044	7036	M	white	53 yr	Double-Blind	MK-0518	800.00 mg	89	Rash pruritic	5 day	279	mild	N	prob not	no action with test drug	recovered
0180060	7013	M	white	37 yr	Double-Blind	MK-0518	800.00 mg	30	**Rash maculopapular**	1.45 mo	279	mild	N	poss	no action with test drug	recovered
Placebo																
0180005	8356	M	white	46 yr	Double-Blind	Placebo	0.00 mg	16	Rash	9 day	219	mild	N	poss	no action with test drug	recovered
						Placebo	0.00 mg	42	Rash	13 day	219	mild	N	def not	no action with test drug	recovered
0180010	8378	M	white	43 yr	Double-Blind	Placebo	0.00 mg	13	Rash maculopapular	25 day	168	mod	N	poss	no action with test drug	recovered
MK-0518 400 mg b.i.d.																

Listing of Patients With Specific Clinical Adverse Experiences of Rash and Related Terms
(Incidence >0% in One or More Treatment Groups) by System Organ Class–Patients Who Received OBT With Darunavir in the Treatment Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Cumulative Data*

Study Number	AN	Gender	Race	Age	Period	Therapy	Total Daily Dose	Relative Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontinuance†	Intensity	Serious	Drug Relationship	Action Taken	Outcome
MK-0518 400 mg b.i.d.																
0190005	16211	M	Hispa	39 yr	Double-Blind	MK-0518	800.00 mg	156	Rash	2.66 mo	281	mild	N	def not	no action with test drug	recovered
0190010	15057	M	white	48 yr	Double-Blind	MK-0518	800.00 mg	107	Rash generalised	9 day	230	mod	N	def not	no action with test drug	recovered
	16276	M	black	21 yr	Double-Blind	MK-0518	800.00 mg	12	Rash	1.22 mo	227	mod	N	def not	no action with test drug	recovered
0190011	16322	M	white	39 yr	Double-Blind	MK-0518	800.00 mg	16	Rash maculo-papular	5.42 mo	224	mild	N	poss	no action with test drug	recovered
0190013	16278	M	Hispa	44 yr	Double-Blind	MK-0518	800.00 mg	148	Rash	3 day	227	mod	N	def not	no action with test drug	recovered
0190021	**15055**	**M**	**white**	**43 yr**	**Double-Blind**	**Off Drug 1 day**		**232**	**Rash macular**	**CONT**	**231**	**mild**	**N**	**prob not**	**no action with test drug**	**not recovered**
	15065	**M**	**white**	**40 yr**	**Double-Blind**	**Off Drug 2 days**		**229**	**Rash**	**CONT**	**227**	**mild**	**N**	**def not**	**no action with test drug**	**not recovered**

Listing of Patients With Specific Clinical Adverse Experiences of Rash and Related Terms
(Incidence >0% in One or More Treatment Groups) by System Organ Class–Patients Who Received OBT With Darunavir in the Treatment Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Cumulative Data*

Study Number	AN	Gender	Race	Age	Period	Therapy	Total Daily Dose	Relative Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontinuance†	Intensity	Serious	Drug Relationship	Action Taken	Outcome
MK-0518 400 mg b.i.d.																
0190023	**16257**	**M**	**white**	**43 yr**	**Double-Blind**	**MK-0518**	**800.00 mg**	**205**	**Rash**	**10 day**	**280**	**mild**	**N**	**def not**	**no action with test drug**	**recovered**
0190027	**16365**	**M**	**black**	**48 yr**	**Double-Blind**	**MK-0518**	**800.00 mg**	**27**	**Rash**	**29 day**	**164**	**mild**	**N**	**prob not**	**no action with test drug**	**recovered**
	16409	**M**	**black**	**43 yr**	**Double-Blind**	**MK-0518**	**800.00 mg**	**54**	**Rash**	**1.97 mo**	**168**	**mild**	**N**	**poss**	**no action with test drug**	**recovered**
0190044	16272	M	white	49 yr	Double-Blind	MK-0518	800.00 mg	8	Rash	3 day	231	mild	N	prob	no action with test drug	recovered
0190045	16291	M	white	56 yr	Double-Blind	MK-0518	800.00 mg	8	Rash	21 day	223	mod	N	prob	no action with test drug	recovered
	16318	M	white	50 yr	Double-Blind	MK-0518	800.00 mg	11	Rash macular	6.28 mo	200	mild	N	def not	no action with test drug	recovered
0190047	15119	M	Hispa	54 yr	Double-Blind	MK-0518	800.00 mg	55	Rash	1.05 mo	168	mod	N	def not	no action with test drug	recovered

Listing of Patients With Specific Clinical Adverse Experiences of Rash and Related Terms
(Incidence >0% in One or More Treatment Groups) by System Organ Class–Patients Who Received OBT With Darunavir in the Treatment Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Cumulative Data*

Study Number	AN	Gender	Race	Age	Period	Therapy	Total Daily Dose	Relative Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontinuance[†]	Intensity	Serious	Drug Relationship	Action Taken	Outcome
MK-0518 400 mg b.i.d.																
0190047	15119	M	Hispa	54 yr	Double-Blind	MK-0518	800.00 mg	86	Rash	30 day	168	mild	N	def not	no action with test drug	recovered
0190048	15029	M	white	52 yr	Double-Blind	MK-0518	800.00 mg	2	Rash	9.43 mo	224	mild	N	def not	no action with test drug	recovered
0190051	**15012**	**M**	**white**	**59 yr**	**Double-Blind**	**MK-0518**	**800.00 mg**	**251**	**Rash maculo-papular**	**CONT**	**280**	**mild**	**N**	**prob not**	**no action with test drug**	**not recovered**
	15040	M	white	51 yr	Double-Blind	MK-0518	800.00 mg	108	Rash	15 day	278	mild	N	def not	no action with test drug	recovered
Placebo																

Listing of Patients With Specific Clinical Adverse Experiences of Rash and Related Terms
(Incidence >0% in One or More Treatment Groups) by System Organ Class–Patients Who Received OBT With Darunavir in the Treatment Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Cumulative Data*

Study Number	AN	Gender	Race	Age	Period	Therapy	Total Daily Dose	Relative Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontinuance[†]	Intensity	Serious	Drug Relationship	Action Taken	Outcome
Placebo																
0190027	**15114**	**M**	**black**	**40 yr**	**Double-Blind**	**Placebo**	**0.00 mg**	**84**	**Rash papular**	**28 day**	**168**	**mild**	**N**	**prob not**	**no action with test drug**	**recovered**
0190032	16399	F	black	41 yr	Double-Blind	Placebo	0.00 mg	80	Rash papular	2.20 mo	170	mild	N	def not	no action with test drug	recovered

[†]Day study therapy was discontinued relative to the start of study therapy.
Drug Relationship: def = definitely, def not = definitely not, poss = possibly, prob = probably, prob not = probably not
Intensity: mod = moderate
Note: MK-0518 and Placebo were administered with Optimized Background Therapy (OBT).
Adverse experience terms are from MedDRA Version 9.1.

[Ref. 5.3.5.1: P005-Define, P018-Define, P019-Define]

Appendix 2.7.4: 66

Number (%) of Patients With Specific Drug-Related Clinical Adverse Experiences of Rash and Related Terms (Incidence >0% in One or More Treatment Groups) by System Organ Class—Related to MK-0518 or Placebo (Alone or in Combination With Optimized Background Therapy)—Patients Who Received OBT With Darunavir in the Treatment Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Cumulative Data*

	MK-0518 400 mg b.i.d. (N = 193)		Placebo (N = 101)		Total (N = 294)	
	n	(%)	n	(%)	n	(%)
Patients With One Or More Adverse Experiences	6	(3.1)	2	(2.0)	8	(2.7)
Patients With No Adverse Experience	187	(96.9)	99	(98.0)	286	(97.3)
Skin And Subcutaneous Tissue Disorders	6	(3.1)	2	(2.0)	8	(2.7)
Rash	3	(1.6)	1	(1.0)	4	(1.4)
Rash Maculo-Papular	3	(1.6)	1	(1.0)	4	(1.4)

Although a patient may have had two or more clinical adverse experiences, the patient is counted only once within a category. The same patient may appear in different categories.

Note: MK-0518 and Placebo were administered with Optimized Background Therapy (OBT).

Adverse experience terms are from MedDRA Version 9.1.

[Ref. 5.3.5.1: P005-Define, P018-Define, P019-Define]

Appendix 2.7.4: 67

Number (%) of Patients With Specific Drug-Related Clinical Adverse Experiences of Rash and Related Terms (Incidence >0% in One or More Treatment Groups) by System Organ Class—Related to MK-0518 or Placebo (Alone or in Combination With Optimized Background Therapy)—Patients Who Received OBT With Darunavir in the Treatment Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Original Application*

	MK-0518 400 mg b.i.d. (N = 192)		Placebo (N = 101)		Total (N = 293)	
	n	(%)	n	(%)	n	(%)
Patients With One Or More Adverse Experiences	5	(2.6)	2	(2.0)	7	(2.4)
Patients With No Adverse Experience	187	(97.4)	99	(98.0)	286	(97.6)
Skin And Subcutaneous Tissue Disorders	5	(2.6)	2	(2.0)	7	(2.4)
Rash	2	(1.0)	1	(1.0)	3	(1.0)
Rash Maculo-Papular	2	(1.0)	1	(1.0)	3	(1.0)
Rash Papular	1	(0.5)	0	(0.0)	1	(0.3)

Although a patient may have had two or more clinical adverse experiences, the patient is counted only once within a category. The same patient may appear in different categories.

Note: MK-0518 and Placebo were administered with Optimized Background Therapy (OBT).

Adverse experience terms are from MedDRA Version 9.1.

[Ref. 5.3.5.1: P005, P018, P019]

Appendix 2.7.4: 68

Listing of Patients With Specific Drug-Related Clinical Adverse Experiences of Rash and Related Terms—Related to MK-0518 or Placebo (Alone or in Combination With Optimized Background Therapy)—Patients Who Received OBT With Darunavir in the Treatment Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Cumulative Data*

Study Number	AN	Gender	Race	Age	Period	Therapy	Total Daily Dose	Relative Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontinuance†	Intensity	Serious	Drug Relationship	Action Taken	Outcome
MK-0518 400 mg b.i.d.																
0180010	7073	M	white	62 yr	Double-Blind	MK-0518	800.00 mg	15	Rash maculo-papular	7 day	224	mod	N	poss	no action with test drug	recovered
0180060	7013	M	white	37 yr	Double-Blind	MK-0518	800.00 mg	30	**Rash maculo-papular**	1.45 mo	279	mild	N	poss	no action with test drug	recovered
Placebo																
0180005	8356	M	white	46 yr	Double-Blind	Placebo	0.00 mg	16	Rash	9 day	219	mild	N	poss	no action with test drug	recovered
0180010	8378	M	white	43 yr	Double-Blind	Placebo	0.00 mg	13	Rash maculo-papular	25 day	168	mod	N	poss	no action with test drug	recovered
MK-0518 400 mg b.i.d.																
0190011	16322	M	white	39 yr	Double-Blind	MK-0518	800.00 mg	16	Rash maculo-papular	5.42 mo	224	mild	N	poss	no action with test drug	recovered

Listing of Patients With Specific Drug-Related Clinical Adverse Experiences of Rash and Related Terms—Related to MK-0518 or Placebo (Alone or in Combination With Optimized Background Therapy)—Patients Who Received OBT With Darunavir in the Treatment Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Cumulative Data*

Study Number	AN	Gender	Race	Age	Period	Therapy	Total Daily Dose	Relative Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontinuance†	Intensity	Serious	Drug Relationship	Action Taken	Outcome
MK-0518 400 mg b.i.d.																
0190027	**16409**	**M**	**black**	**43 yr**	**Double-Blind**	**MK-0518**	**800.00 mg**	**54**	**Rash**	**1.97 mo**	**168**	**mild**	**N**	**poss**	**no action with test drug**	**recovered**
0190044	16272	M	white	49 yr	Double-Blind	MK-0518	800.00 mg	8	Rash	3 day	231	mild	N	prob	no action with test drug	recovered
0190045	16291	M	white	56 yr	Double-Blind	MK-0518	800.00 mg	8	Rash	21 day	223	mod	N	prob	no action with test drug	recovered

†Day study therapy was discontinued relative to the start of study therapy.
Drug Relationship: def = definitely, def not = definitely not, poss = possibly, prob = probably, prob not = probably not
Intensity: mod = moderate
Note: MK-0518 and Placebo were administered with Optimized Background Therapy (OBT).
Adverse experience terms are from MedDRA Version 9.1.

[Ref. 5.3.5.1: P005-Define, P018-Define, P019-Define]

Appendix 2.7.4: 69

Number (%) of Patients With Specific Clinical Adverse Experiences of Rash and Related Terms (Incidence >0% in One or More Treatment Groups) by System Organ Class-Patients Who Received OBT Without Darunavir in the Treatment-Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Cumulative Data*

	MK-0518 400 mg b.i.d. (N = 314)		Placebo (N = 181)		Total (N = 495)	
	n	(%)	n	(%)	n	(%)
Patients With One Or More Adverse Experiences	14	(4.5)	7	(3.9)	21	(4.2)
Patients With No Adverse Experience	300	(95.5)	174	(96.1)	474	(95.8)
Skin And Subcutaneous Tissue Disorders	14	(4.5)	7	(3.9)	21	(4.2)
Rash	9	(2.9)	6	(3.3)	15	(3.0)
Rash Follicular	1	(0.3)	0	(0.0)	1	(0.2)
Rash Macular	1	(0.3)	1	(0.6)	2	(0.4)
Rash Papular	3	(1.0)	0	(0.0)	3	(0.6)
Rash Pruritic	1	(0.3)	0	(0.0)	1	(0.2)

Although a patient may have had two or more clinical adverse experiences, the patient is counted only once within a category. The same patient may appear in different categories.

Note: MK-0518 and Placebo were administered with Optimized Background Therapy (OBT).

Adverse experience terms are from MedDRA Version 9.1.

[Ref. 5.3.5.1: P005-Define, P018-Define, P019-Define]

Appendix 2.7.4: 70

Number (%) of Patients With Specific Clinical Adverse Experiences of Rash and Related Terms (Incidence >0% in One or More Treatment Groups) by System Organ Class–Patients Who Received OBT Without Darunavir in the Treatment Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Original Application*

	MK-0518 400 mg b.i.d. (N = 315)		Placebo (N = 181)		Total (N = 496)	
	n	(%)	n	(%)	n	(%)
Patients With One Or More Adverse Experiences	14	(4.4)	7	(3.9)	21	(4.2)
Patients With No Adverse Experience	301	(95.6)	174	(96.1)	475	(95.8)
Skin And Subcutaneous Tissue Disorders	14	(4.4)	7	(3.9)	21	(4.2)
Rash	9	(2.9)	6	(3.3)	15	(3.0)
Rash Follicular	1	(0.3)	0	(0.0)	1	(0.2)
Rash Macular	1	(0.3)	1	(0.6)	2	(0.4)
Rash Papular	3	(1.0)	0	(0.0)	3	(0.6)
Rash Pruritic	1	(0.3)	0	(0.0)	1	(0.2)

Although a patient may have had two or more clinical adverse experiences, the patient is counted only once within a category. The same patient may appear in different categories.

Note: MK-0518 and Placebo were administered with Optimized Background Therapy (OBT).

Adverse experience terms are from MedDRA Version 9.1.

[Ref. 5.3.5.1: P005, P018, P019]

Appendix 2.7.4: 71

Listing of Patients With Specific Clinical Adverse Experiences of Rash and Related Terms
(Incidence >0% in One or More Treatment Groups) by System Organ Class–Patients Who Received OBT Without Darunavir in the Treatment Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Cumulative Data*

Study Number	AN	Gender	Race	Age	Period	Therapy	Total Daily Dose	Relative Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontinuance[†]	Intensity	Serious	Drug Relationship	Action Taken	Outcome
MK-0518 400 mg b.i.d.																
0050015	3256	M	white	38 yr	Dose-Ranging	MK-0518	800.00 mg	231	Rash papular	1.97 mo	541	mild	N	prob not	no action with test drug	recovered
						MK-0518	800.00 mg	290	Rash follicular	CONT	541	mild	N	prob not	no action with test drug	not recovered
Placebo																
0050021	3241	F	white	41 yr	Dose-Ranging	Placebo	0.00 mg	161	Rash macular	CONT	525	mod	N	poss	no action with test drug	not recovered
0050024	3591	M	white	29 yr	Dose-Ranging	Placebo	0.00 mg	12	Rash	24 day	443	mild	N	prob not	no action with test drug	recovered
MK-0518 400 mg b.i.d.																
0180004	7118	M	white	54 yr	Double-Blind	MK-0518	800.00 mg	11	Rash	4 day	170	mild	N	prob not	no action with test drug	recovered

Listing of Patients With Specific Clinical Adverse Experiences of Rash and Related Terms
(Incidence >0% in One or More Treatment Groups) by System Organ Class–Patients Who Received OBT Without Darunavir in the Treatment Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Cumulative Data*

Study Number	AN	Gen-der	Race	Age	Period	Therapy	Total Daily Dose	Rela-tive Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontin-uance†	Intensity	Ser-ious	Drug Relation-ship	Action Taken	Outcome
MK-0518 400 mg b.i.d.																
0180013	7058	M	white	43 yr	Double-Blind	MK-0518	800.00 mg	1	Rash	3 day	226	mod	N	def	no action with test drug	recovered
0180017	8262	M	white	43 yr	Double-Blind	MK-0518	800.00 mg	82	Rash	4 day	234	mod	N	poss	no action with test drug	recovered
0180024	7010	M	white	50 yr	Double-Blind	MK-0518	800.00 mg	86	Rash	1.25 mo	297	mod	N	prob not	no action with test drug	recovered
0180027	8372	M	white	49 yr	Double-Blind	MK-0518	800.00 mg	63	Rash	1.18 mo	189	mild	N	poss	no action with test drug	recovered
						MK-0518	**800.00 mg**	**151**	**Rash**	**CONT**	**189**	**mild**	**N**	**prob not**	**no action with test drug**	**not recovered**
0180064	7071	M	white	43 yr	Double-Blind	MK-0518	800.00 mg	48	Rash	12 day	224	mild	N	def not	no action with test drug	recovered
Placebo																

Listing of Patients With Specific Clinical Adverse Experiences of Rash and Related Terms
(Incidence >0% in One or More Treatment Groups) by System Organ Class–Patients Who Received OBT Without Darunavir in the Treatment Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Cumulative Data*

Study Number	AN	Gender	Race	Age	Period	Therapy	Total Daily Dose	Relative Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontinuance†	Intensity	Serious	Drug Relationship	Action Taken	Outcome
Placebo																
0180034	8301	M	multi	33 yr	Double-Blind	Placebo	0.00 mg	4	Rash	1.48 mo	246	mild	N	poss	no action with test drug	recovered
0180036	8339	F	multi	35 yr	Double-Blind	Placebo	0.00 mg	10	Rash	1 day	224	mild	N	def not	no action with test drug	recovered
MK-0518 400 mg b.i.d.																
0190014	16247	M	white	45 yr	Double-Blind	MK-0518	800.00 mg	3	Rash papular	12 day	261	mild	N	prob not	no action with test drug	recovered
						MK-0518	800.00 mg	22	Rash papular	2.30 mo	261	mild	N	prob not	no action with test drug	recovered
0190015	16232	M	black	44 yr	Double-Blind	MK-0518	800.00 mg	144	Rash pruritic	CONT	275	mild	N	prob not	no action with test drug	not recovered
0190016	15603	M	black	39 yr	Double-Blind	MK-0518	800.00 mg	42	Rash papular	CONT	280	mild	N	def not	no action with test drug	not recovered

Listing of Patients With Specific Clinical Adverse Experiences of Rash and Related Terms
(Incidence >0% in One or More Treatment Groups) by System Organ Class–Patients Who Received OBT Without Darunavir in the Treatment Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Cumulative Data*

Study Number	AN	Gender	Race	Age	Period	Therapy	Total Daily Dose	Relative Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontinuance†	Intensity	Serious	Drug Relationship	Action Taken	Outcome
MK-0518 400 mg b.i.d.																
0190032	15005	M	white	46 yr	Double-Blind	MK-0518	800.00 mg	41	Rash	1.41 mo	315	mod	N	poss	no action with test drug	recovered
0190035	16353	M	white	22 yr	Double-Blind	MK-0518	800.00 mg	9	Rash macular	9 day	169	mod	N	prob	no action with test drug	recovered
0190037	16302	M	Hispa	33 yr	Double-Blind	MK-0518	800.00 mg	10	Rash	15 day	239	severe	N	prob not	no action with test drug	recovered
0190054	16363	M	white	59 yr	Double-Blind	MK-0518	800.00 mg	79	Rash	2.92 mo	172	mild	N	def not	no action with test drug	recovered
Placebo																

Listing of Patients With Specific Clinical Adverse Experiences of Rash and Related Terms
(Incidence >0% in One or More Treatment Groups) by System Organ Class–Patients Who Received OBT Without Darunavir in the Treatment Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Cumulative Data*

Study Number	AN	Gender	Race	Age	Period	Therapy	Total Daily Dose	Relative Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontinuance[†]	Intensity	Serious	Drug Relationship	Action Taken	Outcome
Placebo																
0190024	15002	M	black	59 yr	Double-Blind	Placebo	0.00 mg	49	Rash	8 day	300	mod	N	poss	no action with test drug	recovered
0190034	16389	M	multi	49 yr	Double-Blind	Placebo	0.00 mg	4	Rash	10 day	167	mild	N	poss	interrupted PRx	recovered
0190035	16355	M	white	52 yr	Double-Blind	Placebo	0.00 mg	11	Rash	11 day	188	mod	N	prob	no action with test drug	recovered

[†]Day study therapy was discontinued relative to the start of study therapy.
Drug Relationship: def = definitely, def not = definitely not, poss = possibly, prob = probably, prob not = probably not
Intensity: mod = moderate
Note: MK-0518 and Placebo were administered with Optimized Background Therapy (OBT).
Adverse experience terms are from MedDRA Version 9.1.

[Ref. 5.3.5.1: P005-Define, P018-Define, P019-Define]

Appendix 2.7.4: 72

Number (%) of Patients With Specific Drug-Related Clinical Adverse Experiences of Rash and Related Terms (Incidence >0% in One or More Treatment Groups) by System Organ Class—Related to MK-0518 or Placebo (Alone or in Combination With Optimized Background Therapy)—Patients Who Received OBT Without Darunavir in the Treatment Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Cumulative Data*

	MK-0518 400 mg b.i.d. (N = 314)		Placebo (N = 181)		Total (N = 495)	
	n	(%)	n	(%)	n	(%)
Patients With One Or More Adverse Experiences	5	(1.6)	5	(2.8)	10	(2.0)
Patients With No Adverse Experience	309	(98.4)	176	(97.2)	485	(98.0)
Skin And Subcutaneous Tissue Disorders	5	(1.6)	5	(2.8)	10	(2.0)
Rash	4	(1.3)	4	(2.2)	8	(1.6)
Rash Macular	1	(0.3)	1	(0.6)	2	(0.4)

Although a patient may have had two or more clinical adverse experiences, the patient is counted only once within a category. The same patient may appear in different categories.

Note: MK-0518 and Placebo were administered with Optimized Background Therapy (OBT).

Adverse experience terms are from MedDRA Version 9.1.

[Ref. 5.3.5.1: P005-Define, P018-Define, P019-Define]

Appendix 2.7.4: 73

Number (%) of Patients With Specific Drug-Related Clinical Adverse Experiences of Rash and Related Terms (Incidence >0% in One or More Treatment Groups) by System Organ Class—Related to MK-0518 or Placebo (Alone or in Combination With Optimized Background Therapy)—Patients Who Received OBT Without Darunavir in the Treatment Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Original Application*

	MK-0518 400 mg b.i.d. (N = 315)		Placebo (N = 181)		Total (N = 496)	
	n	(%)	n	(%)	n	(%)
Patients With One Or More Adverse Experiences	5	(1.6)	5	(2.8)	10	(2.0)
Patients With No Adverse Experience	310	(98.4)	176	(97.2)	486	(98.0)
Skin And Subcutaneous Tissue Disorders	5	(1.6)	5	(2.8)	10	(2.0)
Rash	4	(1.3)	4	(2.2)	8	(1.6)
Rash Macular	1	(0.3)	1	(0.6)	2	(0.4)

Although a patient may have had two or more clinical adverse experiences, the patient is counted only once within a category. The same patient may appear in different categories.

Note: MK-0518 and Placebo were administered with Optimized Background Therapy (OBT).

Adverse experience terms are from MedDRA Version 9.1.

[Ref. 5.3.5.1: P005, P018, P019]

Appendix 2.7.4: 74

Listing of Patients With Specific Drug-Related Clinical Adverse Experiences of Rash and Related Terms—Related to MK-0518 or Placebo (Alone or in Combination With Optimized Background Therapy)—Patients Who Received OBT Without Darunavir in the Treatment Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Cumulative Data*

Study Number	AN	Gen-der	Race	Age	Period	Therapy	Total Daily Dose	Rela-tive Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontin-uance†	Intensity	Ser-ious	Drug Relation-ship	Action Taken	Outcome
Placebo																
0050021	3241	F	white	41 yr	Dose-Ranging	Placebo	0.00 mg	161	Rash macular	CONT	525	mod	N	poss	no action with test drug	not recovered
MK-0518 400 mg b.i.d.																
0180013	7058	M	white	43 yr	Double-Blind	MK-0518	800.00 mg	1	Rash	3 day	226	mod	N	def	no action with test drug	recovered
0180017	8262	M	white	43 yr	Double-Blind	MK-0518	800.00 mg	82	Rash	4 day	234	mod	N	poss	no action with test drug	recovered
0180027	8372	M	white	49 yr	Double-Blind	MK-0518	800.00 mg	63	Rash	1.18 mo	189	mild	N	poss	no action with test drug	recovered
Placebo																
0180034	8301	M	multi	33 yr	Double-Blind	Placebo	0.00 mg	4	Rash	1.48 mo	246	mild	N	poss	no action with test drug	recovered

Listing of Patients With Specific Drug-Related Clinical Adverse Experiences of Rash and Related Terms—Related to MK-0518 or Placebo (Alone or in Combination With Optimized Background Therapy)—Patients Who Received OBT Without Darunavir in the Treatment Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Cumulative Data*

Study Number	AN	Gender	Race	Age	Period	Therapy	Total Daily Dose	Relative Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontinuance[†]	Intensity	Serious	Drug Relationship	Action Taken	Outcome
MK-0518 400 mg b.i.d.																
0190032	15005	M	white	46 yr	Double-Blind	MK-0518	800.00 mg	41	Rash	1.41 mo	315	mod	N	poss	no action with test drug	recovered
0190035	16353	M	white	22 yr	Double-Blind	MK-0518	800.00 mg	9	Rash macular	9 day	169	mod	N	prob	no action with test drug	recovered
Placebo																
0190024	15002	M	black	59 yr	Double-Blind	Placebo	0.00 mg	49	Rash	8 day	300	mod	N	poss	no action with test drug	recovered
0190034	16389	M	multi	49 yr	Double-Blind	Placebo	0.00 mg	4	Rash	10 day	167	mild	N	poss	interrupted PRx	recovered

Listing of Patients With Specific Drug-Related Clinical Adverse Experiences of Rash and Related Terms—Related to MK-0518 or Placebo (Alone or in Combination With Optimized Background Therapy)—Patients Who Received OBT Without Darunavir in the Treatment Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort (Protocols 005, 018, and 019) - *Cumulative Data*

Study Number	AN	Gender	Race	Age	Period	Therapy	Total Daily Dose	Relative Day of Onset	Adverse Experience	Duration of Adverse Experience	Relative Day of Discontinuance[†]	Intensity	Serious	Drug Relationship	Action Taken	Outcome
Placebo																
0190035	16355	M	white	52 yr	Double-Blind	Placebo	0.00 mg	11	Rash	11 day	188	mod	N	prob	no action with test drug	recovered

[†]Day study therapy was discontinued relative to the start of study therapy.
Drug Relationship: def = definitely, def not = definitely not, poss = possibly, prob = probably, prob not = probably not
Intensity: mod = moderate
Note: MK-0518 and Placebo were administered with Optimized Background Therapy (OBT).
Adverse experience terms are from MedDRA Version 9.1.

[Ref. 5.3.5.1: P005-Define, P018-Define, P019-Define]

Appendix 2.7.4: 75

Events by Class of Terms
(Double-Blind Phase, Frozen File)
(Protocols 004, 005, 018, and 019 Combined) - *Original Application*

	MK-0518 (N = 758) 508 Patient-Years		Comparator Group (N = 323) 169 Patient-Years	
	n (%)†	Rate‡	n (%)†	Rate‡
Total number of patients with Endpoint	**10 (1.3)**	**2.0**	**1 (0.3)**	**0.6**
Squamous cell carcinoma	3 (0.4)	0.6	1 (0.3)	0.6
Rectal cancer	1 (0.1)	0.2	0 (0.0)	0.0
Lymphoma	2 (0.3)	0.4	0 (0.0)	0.0
Kaposi's sarcoma	2 (0.3)	0.4	0 (0.0)	0.0
Hepatic neoplasm malignant	1 (0.1)	0.2	0 (0.0)	0.0
B-cell lymphoma	1 (0.1)	0.2	0 (0.0)	0.0

† Crude incidence (100×n/N).

‡ Events per 100 patient-years, with patient-years at risk (PYR) calculated based on the overall endpoint.

Note: Patients with multiple events may be counted more than once in different terms, but only once in one term.

[Ref. 5.3.5.1: P004, P005, P018, P019]

Appendix 2.7.4: 76

Events - Relative Risk and Associated 95% CI
(Double-Blind Phase, Frozen File)
(Protocol 004, 005, 018, and 019 Combined) - *Original Application*

	MK-0518		Comparator Group		Relative Risk[§]
	N	Cases/PYR[†] (Rate[‡])	N	Cases/PYR[†] (Rate[‡])	(95% CI)
Total	758	10/508 (1.970)	323	1/169 (0.592)	3.328 (0.474, 144.446)
Protocol 004	163	0/183 (0.000)	41	1/42 (2.390)	
Protocol 005	133	0/100 (0.000)	45	0/23 (0.000)	
Protocol 018	232	6/114 (5.271)	118	0/52 (0.000)	
Protocol 019	230	4/111 (3.600)	119	0/51 (0.000)	

[†] Patients-years at risk.

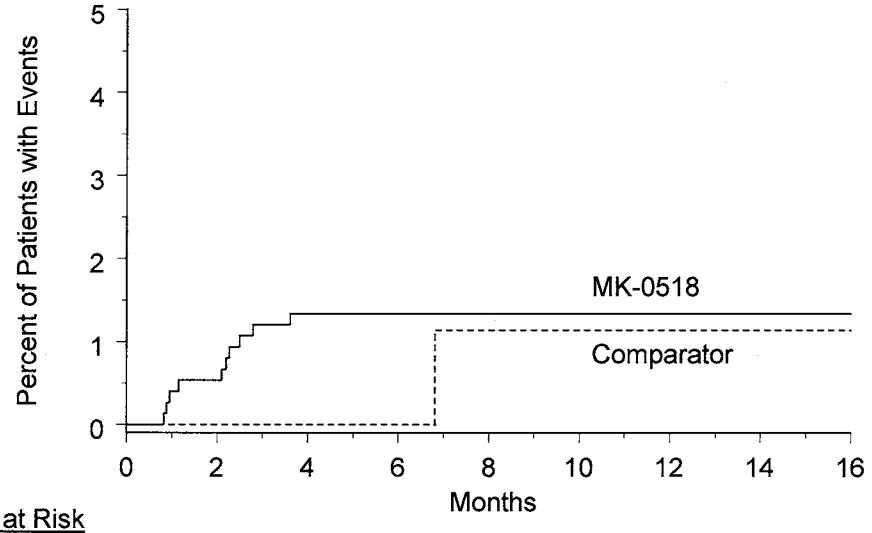
[‡] Per 100 person-years (PYR).

[§] CI based on exact approach using Binomial conditional distribution.

[Ref. 5.3.5.1: P004, P005, P018, P019]

Appendix 2.7.4: 77

Kaplan-Meier Plot of Time to Malignancy
(Double-Blind Phase, Frozen File)
(Protocol 004, 005, 018, and 019 Combined) - *Original Application*



Number at Risk

MK-0518*	758	741	725	493	266	205	155	68	24
Comparator*	323	317	302	123	50	39	32	15	4

*: +OBT for P005, P018 and P019; +3TC +TFV for P004

[Ref. 5.3.5.1: P004, P005, P018, P019]

Appendix 2.7.4: 78

Events by Class of Terms
(Double-Blind + Open-Label + Open-Label Post Virologic Failure, Frozen File)
(Protocols 004, 005, 018, and 019 Combined) - *Original Application*

	MK-0518 (N = 878) 619 Patient-Years		Comparator Group (N = 323) 169 Patient-Years	
	n (%)†	Rate‡	n (%)†	Rate‡
Total number of patients with Endpoint	**12 (1.4)**	**1.9**	**1 (0.3)**	**0.6**
Squamous cell carcinoma	3 (0.3)	0.5	1 (0.3)	0.6
Rectal cancer	1 (0.1)	0.2	0 (0.0)	0.0
Lymphoma	2 (0.2)	0.3	0 (0.0)	0.0
Kaposi's sarcoma	2 (0.2)	0.3	0 (0.0)	0.0
Hodgkin's disease	2 (0.2)	0.3	0 (0.0)	0.0
Hepatic neoplasm malignant	1 (0.1)	0.2	0 (0.0)	0.0
Basal cell carcinoma	1 (0.1)	0.2	0 (0.0)	0.0
B-cell lymphoma	1 (0.1)	0.2	0 (0.0)	0.0

† Crude incidence (100×n/N).

‡ Events per 100 patient-years, with patient-years at risk (PYR) calculated based on the overall endpoint.

Note: Patients with multiple events may be counted more than once in different terms, but only once in one term.

[Ref. 5.3.5.1: P004, P005, P018, P019]

Appendix 2.7.4: 79

Events - Relative Risk and Associated 95% CI
(Double-Blind + Open-Label + Open-Label Post Virologic Failure, Frozen File)
(Protocols 004, 005, 018, and 019 Combined) - *Original Application*

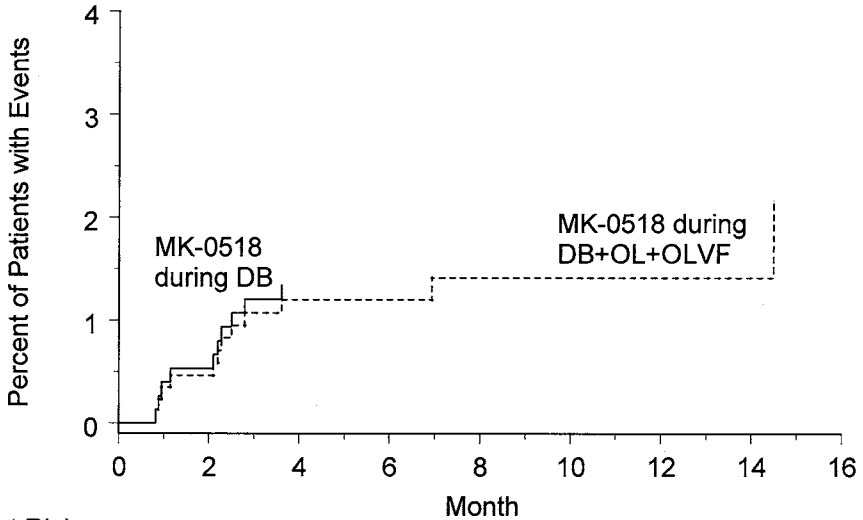
	MK-0518		
	N	Cases/PYR[†] (Rate[‡])	(95% CI)
Total	878	12/619 (1.940)	(1.002, 3.388)
Protocol 004	163	0/183 (0.000)	
Protocol 005	176	2/191 (1.046)	
Protocol 018	274	6/122 (4.899)	
Protocol 019	265	4/122 (3.277)	

[†] Patients-years at risk.
[‡] Per 100 person-years (PYR).

[Ref. 5.3.5.1: P004, P005, P018, P019]

Appendix 2.7.4: 80

Kaplan-Meier Plot of Time to Malignancies
Patients Receiving MK-0518 in Double-Blind Plus Open-Label Extension Plus Open-Label Post Virologic Failure Phases
(Protocols 004, 005, 018, and 019 Combined) - *Original Application*



Number at Risk									
DB*	758	741	725	493	266	205	155	68	24
DB+OL+OLF*	878	829	774	563	336	289	262	153	79

*: on MK-0518

[Ref. 5.3.5.1: P004, P005, P018, P019]

Appendix 2.7.4: 81

All Cause Mortality - Relative Risk and Associated 95% CI
Protocol 004, 005, 018, 019 Combined
(Double-Blind Phase, Frozen File) - *Original Application*

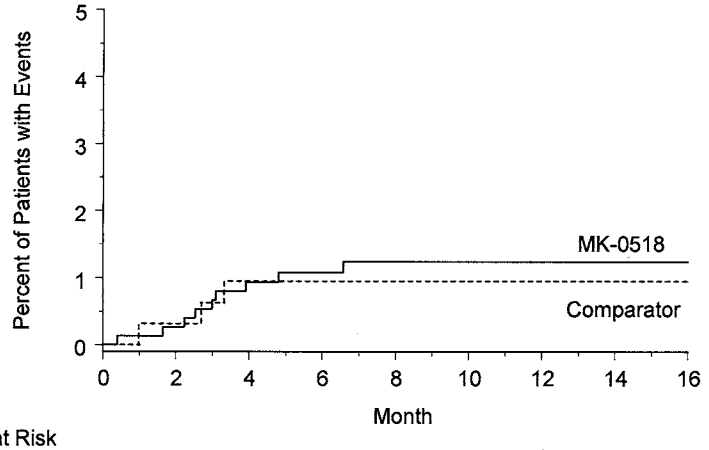
	MK-0518		Control Group		Relative Risk
	N	Cases/PYR† (Rate‡)	N	Cases/PYR† (Rate‡)	(95% CI)
Total	758	8/510 (1.568)	323	3/169 (1.771)	0.885(0.212, 5.180)
Protocol 004	163	0/183 (0.000)	41	0/42 (0.000)	
Protocol 005	133	2/100 (2.004)	45	0/23 (0.000)	
Protocol 018	232	3/116 (2.587)	118	3/52 (5.742)	
Protocol 019	230	3/112 (2.684)	119	0/51 (0.000)	

† Patients-years at risk.
‡ Per 100 person-years (PYR).

[Ref. 5.3.5.1: P004, P005, P018, P019]

Appendix 2.7.4: 82

Kaplan Meier Plot of All Cause Mortality
(Protocol 004, 005, 018, 019: Combined-
Double-Blind Phase, Frozen File) - *Original Application*



Number at Risk									
MK-0518*	758	745	735	676	463	243	154	145	142
Comparator*	323	317	305	191	104	48	35	35	34

*: +OBT for P005, P018 and P019; + 3TC+TFV for P004
[Ref. 5.3.5.1: P004, P005, P018, P019]

Appendix 2.7.4: 83

All Cause Mortality - Relative Risk and Associated 95% CI
(Protocols 004, 005, 018, 019 Combined)
(Double-Blind + Open-Label + Open-Label Post Virologic Failure, Frozen File) -
Original Application

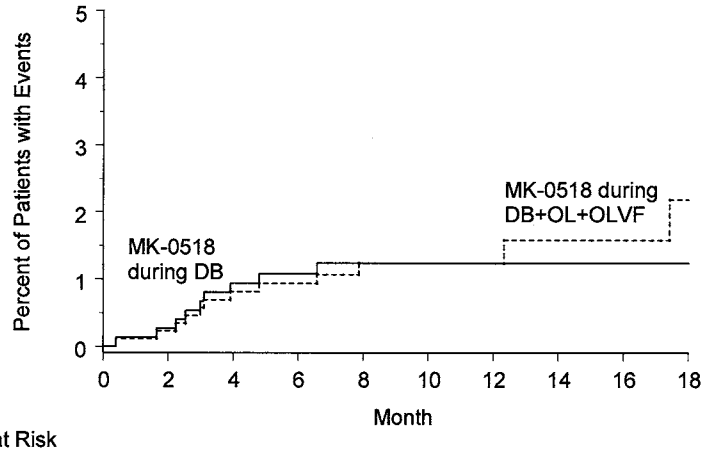
	MK-0518		
	N	Cases/PYR[†](Rate[‡])	(95% CI)
Total	878	10/622 (1.607)	(0.771, 2.955)
Protocol 004	163	0/183 (0.000)	
Protocol 005	176	3/192 (1.563)	
Protocol 018	274	3/125 (2.407)	
Protocol 019	265	4/123 (3.257)	

[†] Patients-years at risk.
[‡] Per 100 person-years (PYR).

[Ref. 5.3.5.1: P004, P005, P018, P019]

Appendix 2.7.4: 84

Kaplan Meier Plot of All Cause Mortality
(Protocols 004, 005, 018, 019 Combined)
(Double-Blind + Open-Label + Open-Label Post Virologic Failure, Frozen File) -
Original Application



Number at Risk

DB*	758	745	735	676	463	243	154	145	142	66
DB+OL+OLF*	902	875	825	778	578	348	288	275	245	140

*: on MK-0518

[Ref. 5.3.5.1: P004, P005, P018, P019]

Appendix 2.7.4: 85

Number (%) of Patients With a Laboratory Predefined Limit of Change (PDLC)† by Treatment Group
(Open-Label Post Virologic Failure Phase - Protocols 005, 018 and 019) - *Cumulative Data*

Laboratory Test (Unit)	PDLC Criteria	Grade	Number (%) With PDLC MK-0518 400 mg b.i.d. (N=208) n/m (%)
hematology laboratory test			
absolute neutrophil count (10[3]/microL)	1.00 - 1.30	Grade 1	18/199 (9.0)
	0.75 - 0.999	Grade 2	7/199 (3.5)
	0.50 - 0.749	Grade 3	3/199 (1.5)
	<0.50	Grade 4	2/199 (1.0)
hemoglobin (gm/dL)	8.5 - 10.0	Grade 1	14/200 (7.0)
	7.5 - 8.4	Grade 2	4/200 (2.0)
	6.5 - 7.4	Grade 3	1/200 (0.5)
	< 6.5	Grade 4	1/200 (0.5)
platelet count (10[3]/microL)	100 - 124.999	Grade 1	12/197 (6.1)
	50 - 99.999	Grade 2	6/197 (3.0)
	25 - 49.999	Grade 3	0/197 (0.0)
	<25	Grade 4	0/197 (0.0)

Number (%) of Patients With a Laboratory Predefined Limit of Change (PDLC)[†] by Treatment Group
(Open-Label Post Virologic Failure Phase - Protocols 005, 018 and 019) - *Cumulative Data*

Laboratory Test (Unit)	PDLC Criteria	Grade	Number (%) With PDLC MK-0518 400 mg b.i.d. (N=208) n/m (%)
blood chemistry test			
fasting(non-random) serum LDL-C (mg/dL)	130 - 159	Grade 1	15/126 (11.9)
	160 - 189	Grade 2	13/126 (10.3)
	≥190	Grade 3	5/126 (4.0)
fasting(non-random) serum cholesterol (mg/dL)	200 - 239	Grade 1	23/145 (15.9)
	240 - 300	Grade 2	19/145 (13.1)
	>300	Grade 3	6/145 (4.1)
fasting(non-random) serum triglyceride (mg/dL)	500 - 750	Grade 2	6/145 (4.1)
	751 - 1200	Grade 3	3/145 (2.1)
	>1200	Grade 4	2/145 (1.4)
fasting(non-random) serum glucose test (mg/dL)	110 -125	Grade 1	16/145 (11.0)
	126 - 250	Grade 2	5/145 (3.4)

Number (%) of Patients With a Laboratory Predefined Limit of Change (PDLC)[†] by Treatment Group
(Open-Label Post Virologic Failure Phase - Protocols 005, 018 and 019) - *Cumulative Data*

Laboratory Test (Unit)	PDLC Criteria	Grade	Number (%) With PDLC MK-0518 400 mg b.i.d. (N=208) n/m (%)
	251 - 500	Grade 3	4/145 (2.8)
	>500	Grade 4	0/145 (0.0)
total serum bilirubin (mg/dL)	1.1 - 1.5 x ULN	Grade 1	11/200 (5.5)
	1.6 - 2.5 x ULN	Grade 2	14/200 (7.0)
	2.6 - 5.0 x ULN	Grade 3	9/200 (4.5)
	>5.0 x ULN	Grade 4	0/200 (0.0)
	>2.5 - 5.0 x Baseline[‡]		12/200 (6.0)
	>5.0 -10.0 x Baseline[‡]		14/200 (7.0)
	>10.0 x Baseline[‡]		1/200 (0.5)
serum direct bilirubin (mg/dL)	>2.5 - 5.0 x Baseline[‡]		5/199 (2.5)
	>5.0 - 10.0 x Baseline[‡]		0/199 (0.0)
	>10.0 x Baseline[‡]		0/199 (0.0)

Number (%) of Patients With a Laboratory Predefined Limit of Change (PDLC)[†] by Treatment Group
(Open-Label Post Virologic Failure Phase - Protocols 005, 018 and 019) - *Cumulative Data*

Laboratory Test (Unit)	PDLC Criteria	Grade	Number (%) With PDLC MK-0518 400 mg b.i.d. (N=208) n/m (%)
serum indirect bilirubin (mg/dL)	>2.5 - 5.0 x Baseline[‡]		6/199 (3.0)
	>5.0 - 10.0 x Baseline[‡]		17/199 (8.5)
	>10.0 x Baseline[‡]		1/199 (0.5)
serum creatinine (mg/dL)	1.1 - 1.3 x ULN	Grade 1	14/200 (7.0)
	1.4 - 1.8 x ULN	Grade 2	2/200 (1.0)
	1.9 - 3.4 x ULN	Grade 3	5/200 (2.5)
	≥3.5 x ULN	Grade 4	0/200 (0.0)
	>2.5 x Baseline[‡]		1/200 (0.5)
serum aspartate aminotransferase (IU(aminot.)/L)	1.25 - 2.5 x ULN	Grade 1	56/199 (28.1)
	2.6 - 5.0 x ULN	Grade 2	7/199 (3.5)
	5.1 - 10.0 x ULN	Grade 3	2/199 (1.0)
	>10.0 x ULN	Grade 4	1/199 (0.5)
	>2.5 - 5.0 x Baseline[‡]		11/199 (5.5)

Number (%) of Patients With a Laboratory Predefined Limit of Change (PDLC)[†] by Treatment Group
(Open-Label Post Virologic Failure Phase - Protocols 005, 018 and 019) - *Cumulative Data*

Laboratory Test (Unit)	PDLC Criteria	Grade	Number (%) With PDLC MK-0518 400 mg b.i.d. (N=208) n/m (%)
	>5.0 x Baseline[‡]		4/199 (2.0)
serum alanine aminotransferase (IU(aminot.)/L)	1.25 - 2.5 x ULN	Grade 1	49/200 (24.5)
	2.6 - 5.0 x ULN	Grade 2	11/200 (5.5)
	5.1 - 10.0 x ULN	Grade 3	2/200 (1.0)
	>10.0 x ULN	Grade 4	0/200 (0.0)
	>2.5 - 5.0 x Baseline[‡]		15/200 (7.5)
	>5.0 x Baseline[‡]		5/200 (2.5)
serum alkaline phosphatase (IU(alk phos)/L)	1.25 - 2.5 x ULN	Grade 1	19/200 (9.5)
	2.6 - 5.0 x ULN	Grade 2	5/200 (2.5)
	5.1 - 10.0 x ULN	Grade 3	0/200 (0.0)
	>10.0 x ULN	Grade 4	0/200 (0.0)
	>2.5 - 5.0 x Baseline[‡]		8/200 (4.0)
	>5.0 x Baseline[‡]		1/200 (0.5)

Number (%) of Patients With a Laboratory Predefined Limit of Change (PDLC)[†] by Treatment Group
(Open-Label Post Virologic Failure Phase - Protocols 005, 018 and 019) - *Cumulative Data*

Laboratory Test (Unit)	PDLC Criteria	Grade	Number (%) With PDLC MK-0518 400 mg b.i.d. (N=208) n/m (%)
serum pancreatic amylase test (IU(amylase)/L)[§]	1.1 - 1.5 x ULN	Grade 1	3/200 (1.5)
	1.6 - 2.0 x ULN	Grade 2	2/200 (1.0)
	2.1 - 5.0 x ULN	Grade 3	5/200 (2.5)
	>5.0 x ULN	Grade 4	0/200 (0.0)
serum lipase test (IU(lipase)/L)	1.1 - 1.5 x ULN	Grade 1	11/200 (5.5)
	1.6 - 3.0 x ULN	Grade 2	3/200 (1.5)
	3.1 - 5.0 x ULN	Grade 3	1/200 (0.5)
	>5.0 x ULN	Grade 4	0/200 (0.0)

[†] For inclusion in this analysis, both a baseline and at least one on-treatment laboratory value had to be present. A patient was included as a Grade X event if his/her highest grade during treatment was X and the laboratory value was worse than baseline.

[‡] A patient was included in the event of '>X-fold Baseline' if his/her highest laboratory value during treatment fell in this category and was more extreme than the upper limit of normal (ULNA).

[§] Defined as (the number of patients meeting the specific serum pancreatic amylase criteria) / (the number of patients with serum amylase test result).

Note: MK-0518 and Placebo were administered with Optimized Background Therapy (OBT).

N = total number of patients randomized in the treatment group.

n/m = number of patients with PDLC/number of patients with laboratory test. For the criteria using baseline, m=number of patients with baseline values for that laboratory test.

LLN = Lower limit of normal range. ULN = Upper limit of normal range.

[Ref. 5.3.5.1: P005-Define, P018-Define, P019-Define]

Appendix 2.7.4: 86

Number (%) of Patients With a Laboratory Predefined Limit of Change (PDLC)[†] by Treatment Group
(Open-Label Post Virologic Failure Phase - Protocols 005, 018 and 019) - *Original Application*

Laboratory Test (Unit)	PDLC Criteria	Grade	Number (%) With PDLC MK-0518 400 mg b.i.d. (N=169) n/m (%)
hematology laboratory test			
absolute neutrophil count (10[3]/microL)	1.00 - 1.30	Grade 1	11/155 (7.1)
	0.75 - 0.999	Grade 2	6/155 (3.9)
	0.50 - 0.749	Grade 3	0/155 (0.0)
	<0.50	Grade 4	0/155 (0.0)
hemoglobin (gm/dL)	8.5 - 10.0	Grade 1	13/155 (8.4)
	7.5 - 8.4	Grade 2	1/155 (0.6)
	6.5 - 7.4	Grade 3	1/155 (0.6)
	< 6.5	Grade 4	1/155 (0.6)
platelet count (10[3]/microL)	100 - 124.999	Grade 1	7/151 (4.6)
	50 - 99.999	Grade 2	3/151 (2.0)
	25 - 49.999	Grade 3	0/151 (0.0)
	<25	Grade 4	0/151 (0.0)

Number (%) of Patients With a Laboratory Predefined Limit of Change (PDLC)† by Treatment Group
(Open-Label Post Virologic Failure Phase - Protocols 005, 018 and 019) - *Original Application*

Laboratory Test (Unit)	PDLC Criteria	Grade	Number (%) With PDLC MK-0518 400 mg b.i.d. (N=169) n/m (%)
blood chemistry test			
fasting(non-random) serum LDL-C (mg/dL)	130 - 159	Grade 1	11/66 (16.7)
	160 - 189	Grade 2	4/66 (6.1)
	≥190	Grade 3	1/66 (1.5)
fasting(non-random) serum cholesterol (mg/dL)	200 - 239	Grade 1	12/71 (16.9)
	240 - 300	Grade 2	6/71 (8.5)
	>300	Grade 3	1/71 (1.4)
fasting(non-random) serum triglyceride (mg/dL)	500 - 750	Grade 2	3/71 (4.2)
	751 - 1200	Grade 3	0/71 (0.0)
	>1200	Grade 4	2/71 (2.8)
fasting(non-random) serum glucose test (mg/dL)	110 -125	Grade 1	10/71 (14.1)
	126 - 250	Grade 2	1/71 (1.4)

Number (%) of Patients With a Laboratory Predefined Limit of Change (PDLC)† by Treatment Group
(Open-Label Post Virologic Failure Phase - Protocols 005, 018 and 019) - *Original Application*

Laboratory Test (Unit)	PDLC Criteria	Grade	Number (%) With PDLC MK-0518 400 mg b.i.d. (N=169) n/m (%)
	251 - 500	Grade 3	1/71 (1.4)
	>500	Grade 4	0/71 (0.0)
total serum bilirubin (mg/dL)	1.1 - 1.5 x ULN	Grade 1	10/155 (6.5)
	1.6 - 2.5 x ULN	Grade 2	10/155 (6.5)
	2.6 - 5.0 x ULN	Grade 3	5/155 (3.2)
	>5.0 x ULN	Grade 4	0/155 (0.0)
	>2.5 - 5.0 x Baseline‡		10/155 (6.5)
	>5.0 -10.0 x Baseline‡		11/155 (7.1)
	>10.0 x Baseline‡		0/155 (0.0)
serum direct bilirubin (mg/dL)	>2.5 - 5.0 x Baseline‡		3/155 (1.9)
	>5.0 - 10.0 x Baseline‡		0/155 (0.0)
	>10.0 x Baseline‡		0/155 (0.0)

Number (%) of Patients With a Laboratory Predefined Limit of Change (PDLC)[†] by Treatment Group
(Open-Label Post Virologic Failure Phase - Protocols 005, 018 and 019) - *Original Application*

Laboratory Test (Unit)	PDLC Criteria	Grade	Number (%) With PDLC MK-0518 400 mg b.i.d. (N=169) n/m (%)
serum indirect bilirubin (mg/dL)	>2.5 - 5.0 x Baseline[‡]		6/155 (3.9)
	>5.0 - 10.0 x Baseline[‡]		13/155 (8.4)
	>10.0 x Baseline[‡]		1/155 (0.6)
serum creatinine (mg/dL)	1.1 - 1.3 x ULN	Grade 1	11/155 (7.1)
	1.4 - 1.8 x ULN	Grade 2	2/155 (1.3)
	1.9 - 3.4 x ULN	Grade 3	2/155 (1.3)
	≥3.5 x ULN	Grade 4	0/155 (0.0)
	>2.5 x Baseline[‡]		0/155 (0.0)
serum aspartate aminotransferase (IU(aminot.)/L)	1.25 - 2.5 x ULN	Grade 1	37/155 (23.9)
	2.6 - 5.0 x ULN	Grade 2	5/155 (3.2)
	5.1 - 10.0 x ULN	Grade 3	1/155 (0.6)
	>10.0 x ULN	Grade 4	0/155 (0.0)
	>2.5 - 5.0 x Baseline[‡]		7/155 (4.5)

Number (%) of Patients With a Laboratory Predefined Limit of Change (PDLC)[†] by Treatment Group
(Open-Label Post Virologic Failure Phase - Protocols 005, 018 and 019) - *Original Application*

Laboratory Test (Unit)	PDLC Criteria	Grade	Number (%) With PDLC MK-0518 400 mg b.i.d. (N=169) n/m (%)
	>5.0 x Baseline[‡]		1/155 (0.6)
serum alanine aminotransferase (IU(aminot.)/L)	1.25 - 2.5 x ULN	Grade 1	29/155 (18.7)
	2.6 - 5.0 x ULN	Grade 2	7/155 (4.5)
	5.1 - 10.0 x ULN	Grade 3	1/155 (0.6)
	>10.0 x ULN	Grade 4	0/155 (0.0)
	>2.5 - 5.0 x Baseline[‡]		7/155 (4.5)
	>5.0 x Baseline[‡]		2/155 (1.3)
serum alkaline phosphatase (IU(alk phos)/L)	1.25 - 2.5 x ULN	Grade 1	12/155 (7.7)
	2.6 - 5.0 x ULN	Grade 2	4/155 (2.6)
	5.1 - 10.0 x ULN	Grade 3	0/155 (0.0)
	>10.0 x ULN	Grade 4	0/155 (0.0)
	>2.5 - 5.0 x Baseline[‡]		5/155 (3.2)
	>5.0 x Baseline[‡]		1/155 (0.6)

Number (%) of Patients With a Laboratory Predefined Limit of Change (PDLC)[†] by Treatment Group
(Open-Label Post Virologic Failure Phase - Protocols 005, 018 and 019) - *Original Application*

Laboratory Test (Unit)	PDLC Criteria	Grade	Number (%) With PDLC MK-0518 400 mg b.i.d. (N=169) n/m (%)
serum pancreatic amylase test (IU(amylase)/L)[§]	1.1 - 1.5 x ULN	Grade 1	3/155 (1.9)
	1.6 - 2.0 x ULN	Grade 2	1/155 (0.6)
	2.1 - 5.0 x ULN	Grade 3	4/155 (2.6)
	>5.0 x ULN	Grade 4	0/155 (0.0)
serum lipase test (IU(lipase)/L)	1.1 - 1.5 x ULN	Grade 1	8/155 (5.2)
	1.6 - 3.0 x ULN	Grade 2	2/155 (1.3)
	3.1 - 5.0 x ULN	Grade 3	1/155 (0.6)
	>5.0 x ULN	Grade 4	0/155 (0.0)

[†] For inclusion in this analysis, both a baseline and at least one on-treatment laboratory value had to be present. A patient was included as a Grade X event if his/her highest grade during treatment was X and the laboratory value was worse than baseline.

[‡] A patient was included in the event of '>X-fold Baseline' if his/her highest laboratory value during treatment fell in this category and was more extreme than the upper limit of normal (ULNA).

§ Defined as (the number of patients meeting the specific serum pancreatic amylase criteria) / (the number of patients with serum amylase test result).

Note: MK-0518 and Placebo were administered with Optimized Background Therapy (OBT).

N = total number of patients randomized in the treatment group.

n/m = number of patients with PDLC/number of patients with laboratory test. For the criteria using baseline, m=number of patients with baseline values for that laboratory test.

LLN = Lower limit of normal range. ULN = Upper limit of normal range.

[Ref. 5.3.5.1: P005, P018, P019]

Appendix 2.7.4: 87

Summary of Laboratory Tests
Treatment-Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort
(Protocols 005, 018 and 019) - *Cumulative Data*

	MK-0518 400 mg b.i.d.			Placebo		
Week	N	Baseline Mean	Mean Change[†](SD)	N	Baseline Mean	Mean Change[†](SD)
Absolute neutrophil count (10[3]/microL)						
0	503	2.45		280	2.37	
2	481	2.44	0.68 (1.56)	271	2.37	0.63 (1.85)
4	496	2.47	0.57 (1.77)	276	2.37	0.33 (1.16)
8	490	2.47	0.53 (2.09)	274	2.39	0.28 (1.21)
12	484	2.45	0.53 (1.86)	264	2.37	0.50 (1.46)
16	485	2.46	0.71 (2.19)	267	2.39	0.50 (2.15)
24	433	2.48	0.68 (1.76)	146	2.51	0.51 (1.24)
32	275	2.50	0.88 (2.07)	83	2.55	0.82 (1.31)
40	110	2.41	0.89 (2.12)	30	2.60	0.88 (2.36)
48	5	2.63	0.74 (1.20)			
Fasting(non-random) serum HDL-C (mg/dL)						
0	487	35.65		270	36.46	
12	461	35.69	2.78 (8.78)	251	36.65	1.36 (9.56)
24	418	35.90	3.83 (10.30)	147	37.27	0.63 (9.67)
48	5	30.60	10.20 (10.16)			
Fasting(non-random) serum LDL-C (mg/dL)						
0	401	97.61		226	100.43	
12	342	98.23	12.79 (30.28)	187	103.53	3.34 (32.32)
24	321	100.15	16.60 (29.54)	117	108.47	8.84 (36.92)
48	5	92.20	31.20 (35.05)			
Fasting(non-random) serum cholesterol (mg/dL)						
0	501	179.44		279	183.51	
12	481	179.25	16.38 (45.99)	262	183.78	8.08 (43.88)
24	436	180.31	23.09 (49.19)	149	190.47	11.64 (44.04)
48	5	167.00	40.20 (41.01)			
Fasting(non-random) serum glucose test (mg/dL)						
0	506	96.98		281	97.85	
12	491	97.16	4.77 (29.95)	268	97.35	3.12 (20.24)
24	442	97.37	2.95 (24.65)	149	96.75	0.85 (15.44)
48	5	85.00	6.20 (7.12)			
Fasting(non-random) serum triglyceride (mg/dL)						
0	501	288.69		279	291.89	
12	481	288.65	-18.35 (272.47)	261	292.33	-3.69 (286.04)

Summary of Laboratory Tests
Treatment-Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort
(Protocols 005, 018 and 019) - *Cumulative Data*

	MK-0518 400 mg b.i.d.			Placebo		
Week	N	Baseline Mean	Mean Change[†](SD)	N	Baseline Mean	Mean Change[†](SD)
24	436	285.64	-4.25 (331.47)	149	260.96	4.89 (216.11)
48	5	221.20	-6.60 (70.93)			
Hemoglobin (gm/dL)						
0	505	13.44		280	13.49	
2	484	13.44	-0.13 (0.72)	272	13.54	-0.18 (0.87)
4	498	13.44	0.07 (0.91)	276	13.54	-0.08 (1.00)
8	491	13.49	0.21 (1.15)	274	13.53	-0.04 (1.36)
12	486	13.47	0.32 (1.34)	264	13.52	0.03 (1.29)
16	488	13.49	0.38 (1.36)	268	13.54	0.02 (1.40)
24	434	13.51	0.56 (1.34)	146	13.75	0.28 (1.55)
32	276	13.60	0.57 (1.40)	84	13.52	0.56 (1.74)
40	111	13.82	0.58 (1.50)	30	14.00	0.34 (1.71)
48	5	13.30	0.94 (1.58)			
Platelet count (10[3]/microL)						
0	498	191.66		276	191.90	
2	470	191.14	25.90 (49.76)	263	192.54	23.81 (50.67)
4	484	191.65	30.46 (54.42)	265	192.79	20.83 (49.64)
8	475	192.83	30.58 (57.56)	260	192.32	22.27 (54.97)
12	471	190.83	31.85 (56.17)	255	193.17	16.60 (56.38)
16	477	191.72	32.03 (60.52)	258	193.91	16.95 (54.21)
24	413	192.50	31.61 (57.54)	138	196.64	21.75 (64.26)
32	269	189.09	39.85 (52.95)	79	198.22	24.20 (64.54)
40	108	181.11	50.09 (46.17)	30	212.93	10.73 (63.54)
48	5	199.20	90.60 (76.58)			
Serum alanine aminotransferase (IU(aminotransferase)/L)						
0	507	39.63		281	39.95	
2	490	39.67	-0.21 (26.70)	278	39.99	-0.60 (26.56)
4	501	39.50	-0.38 (30.27)	279	39.89	-0.24 (30.35)
8	500	39.57	-2.08 (30.89)	279	39.49	-3.87 (24.90)
12	492	39.75	-1.60 (46.52)	270	39.98	-3.34 (27.95)
16	492	39.08	-1.82 (33.01)	270	39.61	-1.92 (33.64)
24	442	39.03	-0.53 (54.96)	151	41.19	-1.15 (75.89)
32	289	39.07	-2.12 (29.27)	85	44.94	-7.59 (36.84)
40	116	41.64	-6.90 (23.83)	31	43.87	1.81 (79.56)

Summary of Laboratory Tests
Treatment-Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort
(Protocols 005, 018 and 019) - *Cumulative Data*

	MK-0518 400 mg b.i.d.			Placebo		
Week	N	Baseline Mean	Mean Change[†](SD)	N	Baseline Mean	Mean Change[†](SD)
48	5	29.80	-2.20 (24.47)			
Serum alkaline phosphatase (IU(alk phos)/L)						
0	507	110.50		282	106.30	
2	491	110.89	-5.58 (43.98)	280	106.44	-0.70 (62.62)
4	502	110.39	-0.68 (42.34)	280	104.19	-2.06 (32.95)
8	500	109.85	-1.52 (46.80)	279	106.15	-0.95 (50.99)
12	497	110.62	-0.88 (65.95)	271	103.56	1.30 (55.85)
16	494	109.89	-0.84 (44.07)	271	103.37	-1.45 (37.25)
24	444	109.68	1.61 (69.96)	151	102.28	0.95 (26.57)
32	292	108.25	2.21 (71.85)	85	108.54	-4.31 (34.75)
40	117	106.44	1.27 (51.78)	31	100.29	0.97 (23.17)
48	5	95.00	-1.40 (28.38)			
Serum aspartate aminotransferase (IU(aminotransferase)/L)						
0	507	38.37		280	38.59	
2	480	38.47	-1.38 (20.39)	274	38.31	-1.64 (26.66)
4	498	38.33	-2.28 (23.79)	277	38.03	-0.78 (26.93)
8	496	38.37	-4.33 (20.92)	275	37.35	-3.91 (22.37)
12	488	38.41	-3.87 (30.10)	265	37.57	-3.55 (25.17)
16	483	37.75	-2.72 (28.35)	266	37.93	-3.48 (25.69)
24	439	38.11	-3.85 (49.04)	150	37.61	-4.33 (38.34)
32	283	38.05	-4.62 (23.73)	84	39.69	-8.80 (23.62)
40	114	38.64	-5.28 (25.19)	31	40.06	-3.87 (38.90)
48	5	31.20	-5.40 (9.81)			
Serum creatinine (mg/dL)						
0	507	0.94		282	0.95	
2	491	0.95	0.03 (0.15)	280	0.95	0.02 (0.15)
4	502	0.94	0.03 (0.15)	280	0.95	0.01 (0.12)
8	500	0.94	0.04 (0.18)	279	0.95	0.02 (0.14)
12	498	0.94	0.04 (0.17)	271	0.94	0.03 (0.14)
16	494	0.94	0.04 (0.18)	271	0.94	0.02 (0.14)
24	445	0.95	0.05 (0.17)	151	0.96	0.03 (0.15)
32	292	0.92	0.04 (0.17)	85	0.96	0.03 (0.14)
40	117	0.92	0.10 (0.29)	31	0.99	0.09 (0.14)
48	5	0.78	0.08 (0.08)			

Summary of Laboratory Tests
Treatment-Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort
(Protocols 005, 018 and 019) - *Cumulative Data*

	MK-0518 400 mg b.i.d.			Placebo		
Week	N	Baseline Mean	Mean Change[†](SD)	N	Baseline Mean	Mean Change[†](SD)
Serum direct bilirubin (mg/dL)						
0	507	0.17		280	0.18	
2	481	0.17	0.00 (0.11)	276	0.18	-0.01 (0.11)
4	500	0.17	0.01 (0.17)	275	0.17	-0.01 (0.12)
8	495	0.17	0.00 (0.14)	276	0.17	-0.01 (0.13)
12	487	0.17	0.01 (0.42)	268	0.17	0.00 (0.17)
16	483	0.17	0.01 (0.37)	266	0.17	-0.01 (0.12)
24	439	0.17	0.01 (0.17)	150	0.17	-0.00 (0.12)
32	284	0.17	0.00 (0.11)	85	0.16	0.01 (0.11)
40	114	0.18	0.02 (0.14)	31	0.14	0.01 (0.09)
48	5	0.16	0.02 (0.16)			
Serum indirect bilirubin (mg/dL)						
0	507	0.48		280	0.53	
2	479	0.48	-0.03 (0.66)	276	0.53	-0.10 (0.63)
4	499	0.48	-0.02 (0.62)	275	0.51	-0.05 (0.61)
8	495	0.49	0.00 (0.73)	276	0.52	-0.06 (0.64)
12	487	0.49	-0.00 (0.68)	268	0.53	-0.06 (0.67)
16	483	0.49	-0.00 (0.66)	265	0.53	-0.07 (0.70)
24	439	0.49	-0.01 (0.64)	150	0.55	-0.08 (0.74)
32	284	0.51	-0.04 (0.72)	85	0.52	-0.08 (0.76)
40	114	0.52	0.11 (1.22)	31	0.50	-0.10 (0.72)
48	5	0.52	0.20 (0.87)			
Serum lipase test (IU(lipase)/L)						
0	507	43.32		282	42.50	
2	491	43.56	3.22 (34.45)	280	42.55	1.56 (17.83)
4	502	43.34	2.48 (30.66)	280	42.35	2.04 (20.54)
8	500	43.36	4.05 (52.42)	279	42.35	0.25 (22.17)
12	497	43.54	0.72 (31.50)	271	42.31	0.39 (21.23)
16	494	43.65	0.94 (30.80)	271	42.18	0.97 (24.69)
24	444	44.26	-0.79 (32.36)	151	42.86	0.07 (31.16)
32	292	43.87	2.16 (25.10)	85	40.33	5.98 (38.60)
40	117	43.67	0.89 (19.35)	31	40.52	4.58 (29.15)
48	5	51.20	-4.40 (8.20)			
Total serum bilirubin (mg/dL)						

Summary of Laboratory Tests
Treatment-Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort
(Protocols 005, 018 and 019) - *Cumulative Data*

	MK-0518 400 mg b.i.d.			Placebo		
Week	N	Baseline Mean	Mean Change[†](SD)	N	Baseline Mean	Mean Change[†](SD)
0	507	0.63		281	0.68	
2	490	0.63	-0.01 (0.74)	280	0.69	-0.10 (0.71)
4	502	0.63	-0.02 (0.72)	280	0.68	-0.07 (0.73)
8	500	0.63	-0.00 (0.81)	279	0.68	-0.09 (0.76)
12	494	0.63	0.01 (0.92)	270	0.68	-0.05 (0.77)
16	494	0.63	0.01 (0.86)	270	0.68	-0.08 (0.79)
24	445	0.64	0.00 (0.74)	151	0.70	-0.07 (0.83)
32	292	0.66	-0.04 (0.79)	85	0.65	-0.06 (0.84)
40	117	0.68	0.13 (1.29)	31	0.62	-0.09 (0.78)
48	5	0.68	0.18 (1.06)			

[†]Change Scores are mean change from baseline and are based on the measurements of the patients who were measured at baseline and the time point assessed.

Note: MK-0518 and Placebo were administered with Optimized Background Therapy (OBT).

[Ref. 5.3.5.1: P005-Define, P018-Define, P019-Define]

Appendix 2.7.4: 88

Summary of Laboratory Tests
Treatment-Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort
(Protocols 005, 018 and 019) - *Original Application*

	MK-0518 400 mg b.i.d.			Placebo		
Week	N	Baseline Mean	Mean Change†(SD)	N	Baseline Mean	Mean Change†(SD)
Absolute neutrophil count (10[3]/microL)						
0	503	2.45		280	2.37	
2	481	2.44	0.68 (1.56)	271	2.37	0.63 (1.85)
4	496	2.47	0.57 (1.77)	276	2.37	0.33 (1.16)
8	490	2.47	0.53 (2.09)	274	2.39	0.28 (1.21)
12	484	2.45	0.53 (1.86)	264	2.37	0.50 (1.46)
16	484	2.46	0.71 (2.19)	268	2.39	0.51 (2.14)
24	284	2.52	0.51 (1.87)	91	2.55	0.47 (1.23)
Fasting(non-random) serum HDL-C (mg/dL)						
0	487	35.65		270	36.46	
12	461	35.69	2.78 (8.78)	251	36.65	1.36 (9.56)
24	277	35.18	4.71 (10.34)	91	37.19	2.51 (9.45)
Fasting(non-random) serum LDL-C (mg/dL)						
0	401	97.61		226	100.43	
12	342	98.23	12.79 (30.28)	187	103.53	3.34 (32.32)
24	212	99.91	17.56 (28.82)	74	110.62	7.24 (37.48)
Fasting(non-random) serum cholesterol (mg/dL)						
0	501	179.44		279	183.51	
12	481	179.25	16.38 (45.99)	262	183.78	8.08 (43.88)
24	291	178.53	23.59 (50.27)	93	194.06	10.62 (43.24)
Fasting(non-random) serum glucose test (mg/dL)						
0	506	96.98		281	97.85	
12	491	97.16	4.77 (29.95)	268	97.35	3.12 (20.24)
24	290	97.95	3.17 (21.72)	92	96.20	2.68 (17.99)
Fasting(non-random) serum triglyceride (mg/dL)						
0	501	288.69		279	291.89	
12	481	288.65	-18.35 (272.47)	261	292.33	-3.69 (286.04)
24	291	293.54	-11.46 (350.33)	93	257.01	19.82 (201.82)
Hemoglobin (gm/dL)						
0	505	13.44		280	13.49	
2	484	13.44	-0.13 (0.72)	272	13.54	-0.18 (0.87)
4	498	13.44	0.07 (0.91)	276	13.54	-0.08 (1.00)
8	491	13.49	0.21 (1.15)	274	13.53	-0.04 (1.36)
12	486	13.47	0.32 (1.34)	264	13.52	0.03 (1.29)

Summary of Laboratory Tests
Treatment-Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort
(Protocols 005, 018 and 019) - *Original Application*

	MK-0518 400 mg b.i.d.			Placebo		
Week	N	Baseline Mean	Mean Change[†](SD)	N	Baseline Mean	Mean Change[†](SD)
16	487	13.49	0.38 (1.36)	269	13.54	0.02 (1.40)
24	285	13.56	0.55 (1.40)	91	13.72	0.34 (1.32)
Platelet count (10[3]/microL)						
0	498	191.66		276	191.90	
2	470	191.14	25.90 (49.76)	263	192.54	23.81 (50.67)
4	484	191.65	30.46 (54.42)	265	192.79	20.83 (49.64)
8	475	192.83	30.58 (57.56)	260	192.32	22.27 (54.97)
12	471	190.83	31.85 (56.17)	255	193.17	16.60 (56.38)
16	475	191.36	31.97 (60.53)	259	193.73	16.93 (54.11)
24	273	191.23	30.88 (51.19)	87	205.68	16.05 (71.02)
Serum alanine aminotransferase (IU(aminotransferase)/L)						
0	507	39.63		281	39.95	
2	490	39.67	-0.21 (26.70)	278	39.99	-0.60 (26.56)
4	501	39.50	-0.38 (30.27)	279	39.89	-0.24 (30.35)
8	500	39.57	-2.08 (30.89)	279	39.49	-3.87 (24.90)
12	492	39.75	-1.60 (46.52)	270	39.98	-3.34 (27.95)
16	492	39.08	-1.82 (33.01)	271	39.56	-1.88 (33.58)
24	291	39.23	1.77 (62.11)	93	45.51	-12.14 (25.34)
Serum alkaline phosphatase (IU(alk phos)/L)						
0	507	110.50		282	106.30	
2	491	110.89	-5.58 (43.98)	280	106.44	-0.70 (62.62)
4	502	110.39	-0.68 (42.34)	280	104.19	-2.06 (32.95)
8	500	109.85	-1.52 (46.80)	279	106.15	-0.95 (50.99)
12	497	110.62	-0.88 (65.95)	271	103.56	1.30 (55.85)
16	494	109.89	-0.84 (44.07)	272	103.57	-1.55 (37.22)
24	292	108.26	2.22 (66.93)	93	104.09	-0.68 (21.30)
Serum aspartate aminotransferase (IU(aminotransferase)/L)						
0	507	38.37		280	38.59	
2	480	38.47	-1.38 (20.38)	274	38.31	-1.64 (26.66)
4	498	38.33	-2.28 (23.79)	277	38.03	-0.78 (26.93)
8	496	38.37	-4.33 (20.92)	275	37.35	-3.91 (22.37)
12	488	38.41	-3.87 (30.10)	265	37.57	-3.55 (25.17)
16	483	37.75	-2.72 (28.35)	267	37.88	-3.43 (25.66)
24	288	38.50	-2.21 (58.69)	92	40.29	-9.88 (21.12)

Summary of Laboratory Tests
Treatment-Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort
(Protocols 005, 018 and 019) - *Original Application*

	MK-0518 400 mg b.i.d.			Placebo		
Week	N	Baseline Mean	Mean Change[†](SD)	N	Baseline Mean	Mean Change[†](SD)
Serum creatinine (mg/dL)						
0	507	0.94		282	0.95	
2	491	0.95	0.03 (0.15)	280	0.95	0.02 (0.15)
4	502	0.94	0.03 (0.15)	280	0.95	0.01 (0.12)
8	500	0.94	0.04 (0.18)	279	0.95	0.02 (0.14)
12	498	0.94	0.04 (0.17)	271	0.94	0.03 (0.14)
16	494	0.94	0.04 (0.18)	272	0.94	0.02 (0.14)
24	293	0.93	0.05 (0.17)	93	0.95	0.03 (0.14)
Serum direct bilirubin (mg/dL)						
0	507	0.17		280	0.18	
2	481	0.17	0.00 (0.11)	276	0.18	-0.01 (0.11)
4	500	0.17	0.01 (0.17)	275	0.17	-0.01 (0.12)
8	495	0.17	0.00 (0.14)	276	0.17	-0.01 (0.13)
12	487	0.17	0.01 (0.42)	268	0.17	0.00 (0.17)
16	483	0.17	0.01 (0.37)	267	0.17	-0.01 (0.12)
24	288	0.17	0.02 (0.19)	92	0.16	0.00 (0.12)
Serum indirect bilirubin (mg/dL)						
0	507	0.48		280	0.53	
2	479	0.48	-0.03 (0.66)	276	0.53	-0.10 (0.63)
4	499	0.48	-0.02 (0.62)	275	0.51	-0.05 (0.61)
8	495	0.49	0.00 (0.73)	276	0.52	-0.06 (0.64)
12	487	0.49	-0.00 (0.68)	268	0.53	-0.06 (0.67)
16	483	0.49	-0.00 (0.66)	266	0.53	-0.07 (0.70)
24	288	0.50	-0.01 (0.68)	92	0.48	0.01 (0.64)
Serum lipase test (IU(lipase)/L)						
0	507	43.32		282	42.50	
2	491	43.56	3.22 (34.45)	280	42.55	1.56 (17.83)
4	502	43.34	2.47 (30.67)	280	42.35	2.04 (20.54)
8	500	43.36	4.05 (52.42)	279	42.35	0.25 (22.17)
12	497	43.54	0.72 (31.50)	271	42.31	0.39 (21.23)
16	494	43.65	0.94 (30.80)	272	42.13	0.99 (24.65)
24	292	43.97	0.00 (20.27)	93	39.17	2.73 (34.83)
Total serum bilirubin (mg/dL)						
0	507	0.63		281	0.68	

Summary of Laboratory Tests
Treatment-Experienced MK-0518 400 mg b.i.d. Double-Blind Cohort
(Protocols 005, 018 and 019) - *Original Application*

	MK-0518 400 mg b.i.d.			Placebo		
Week	N	Baseline Mean	Mean Change[†](SD)	N	Baseline Mean	Mean Change[†](SD)
2	490	0.63	-0.01 (0.74)	280	0.69	-0.10 (0.71)
4	502	0.63	-0.02 (0.72)	280	0.68	-0.07 (0.73)
8	500	0.63	-0.00 (0.81)	279	0.68	-0.09 (0.76)
12	494	0.63	0.01 (0.92)	270	0.68	-0.05 (0.77)
16	494	0.63	0.01 (0.86)	271	0.68	-0.07 (0.79)
24	293	0.65	0.01 (0.79)	93	0.61	0.02 (0.74)

[†] Change Scores are mean change from baseline and are based on the measurements of the patients who were measured at baseline and the time point assessed.

Note: MK-0518 and Placebo were administered with Optimized Background Therapy (OBT).

[Ref. 5.3.5.1: P005, P018, P019]