## 付録 2.7.4-123 臨床検査値の Grade がベースラインより悪化した患者の要約
## 001 試験パート B3（APaT 集団）

| Laboratory Test | MK-3475 10 mg/kg Q3W (N=121) | MK-3475 10 mg/kg Q2W (N=123) | Total (N=244) |
|---|---|---|---|
| **APTT Increased** | | | |
| Improved from baseline | 0 (0.0) | 1 (0.8) | 1 (0.4) |
| Worsened from baseline | 2 (1.7) | 4 (3.3) | 6 (2.5) |
| Clinically meaningful† worsened from baseline | 0 (0.0) | 1 (0.8) | 1 (0.4) |
| **Alanine Aminotransferase Increased** | | | |
| Improved from baseline | 1 (0.8) | 1 (0.8) | 2 (0.8) |
| Worsened from baseline | 20 (16.5) | 24 (19.5) | 44 (18.0) |
| Clinically meaningful† worsened from baseline | 2 (1.7) | 3 (2.4) | 5 (2.0) |
| **Albumin Decreased** | | | |
| Improved from baseline | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Worsened from baseline | 33 (27.3) | 40 (32.5) | 73 (29.9) |
| Clinically meaningful† worsened from baseline | 6 (5.0) | 12 (9.8) | 18 (7.4) |
| **Alkaline Phosphatase Increased** | | | |
| Improved from baseline | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Worsened from baseline | 14 (11.6) | 27 (22.0) | 41 (16.8) |
| Clinically meaningful† worsened from baseline | 4 (3.3) | 3 (2.4) | 7 (2.9) |
| **Aspartate Aminotransferase Increased** | | | |
| Improved from baseline | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Worsened from baseline | 26 (21.5) | 33 (26.8) | 59 (24.2) |
| Clinically meaningful† worsened from baseline | 7 (5.8) | 3 (2.4) | 10 (4.1) |
| **Bilirubinn Increased** | | | |



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## 付録 2.7.4-123 臨床検査値の Grade がベースラインより悪化した患者の要約
## 001 試験パート B3（APaT 集団）（続き）

| Laboratory Test | MK-3475 10 mg/kg Q3W (N=121) | MK-3475 10 mg/kg Q2W (N=123) | Total (N=244) |
|---|---|---|---|
| **Bilirubinn Increased** | | | |
| Improved from baseline | 1 (0.8) | 0 (0.0) | 1 (0.4) |
| Worsened from baseline | 9 (7.4) | 14 (11.4) | 23 (9.4) |
| Clinically meaningful† worsened from baseline | 4 (3.3) | 5 (4.1) | 9 (3.7) |
| **Calcium Decreased** | | | |
| Improved from baseline | 0 (0.0) | 1 (0.8) | 1 (0.4) |
| Worsened from baseline | 25 (20.7) | 24 (19.5) | 49 (20.1) |
| Clinically meaningful† worsened from baseline | 2 (1.7) | 7 (5.7) | 9 (3.7) |
| **Cholesterol** | | | |
| Improved from baseline | 1 (0.8) | 0 (0.0) | 1 (0.4) |
| Worsened from baseline | 22 (18.2) | 17 (13.8) | 39 (16.0) |
| Clinically meaningful† worsened from baseline | 3 (2.5) | 1 (0.8) | 4 (1.6) |
| **Creatinine Increased** | | | |
| Improved from baseline | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Worsened from baseline | 12 (9.9) | 20 (16.3) | 32 (13.1) |
| Clinically meaningful† worsened from baseline | 2 (1.7) | 0 (0.0) | 2 (0.8) |
| **Glucose Decreased** | | | |
| Improved from baseline | 0 (0.0) | 1 (0.8) | 1 (0.4) |
| Worsened from baseline | 7 (5.8) | 6 (4.9) | 13 (5.3) |
| Clinically meaningful† worsened from baseline | 1 (0.8) | 0 (0.0) | 1 (0.4) |
| **Glucose Increased** | | | |



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## 付録 2.7.4-123 臨床検査値の Grade がベースラインより悪化した患者の要約
## 001 試験パート B3（APaT 集団）（続き）

| Laboratory Test | MK-3475 10 mg/kg Q3W (N=121) | MK-3475 10 mg/kg Q2W (N=123) | Total (N=244) |
|---|---|---|---|
| **Glucose Increased** | | | |
| Improved from baseline | 1 (0.8) | 2 (1.6) | 3 (1.2) |
| Worsened from baseline | 49 (40.5) | 58 (47.2) | 107 (43.9) |
| Clinically meaningful† worsened from baseline | 11 (9.1) | 13 (10.6) | 24 (9.8) |
| **Hemoglobin Decreased** | | | |
| Improved from baseline | 1 (0.8) | 0 (0.0) | 1 (0.4) |
| Worsened from baseline | 43 (35.5) | 52 (42.3) | 95 (38.9) |
| Clinically meaningful† worsened from baseline | 6 (5.0) | 7 (5.7) | 13 (5.3) |
| **Leukocytes Decreased** | | | |
| Improved from baseline | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Worsened from baseline | 21 (17.4) | 17 (13.8) | 38 (15.6) |
| Clinically meaningful† worsened from baseline | 4 (3.3) | 2 (1.6) | 6 (2.5) |
| **Lymphocytes Decreased** | | | |
| Improved from baseline | 0 (0.0) | 3 (2.4) | 3 (1.2) |
| Worsened from baseline | 32 (26.4) | 27 (22.0) | 59 (24.2) |
| Clinically meaningful† worsened from baseline | 13 (10.7) | 13 (10.6) | 26 (10.7) |
| **Magnesium Decreased** | | | |
| Improved from baseline | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Worsened from baseline | 16 (13.2) | 22 (17.9) | 38 (15.6) |
| Clinically meaningful† worsened from baseline | 1 (0.8) | 2 (1.6) | 3 (1.2) |
| **Magnesium Increased** | | | |



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## 付録 2.7.4-123 臨床検査値の Grade がベースラインより悪化した患者の要約
## 001 試験パート B3（APaT 集団）（続き）

| Laboratory Test | MK-3475 10 mg/kg Q3W (N=121) | MK-3475 10 mg/kg Q2W (N=123) | Total (N=244) |
|---|---|---|---|
| **Magnesium Increased** | | | |
| Improved from baseline | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Worsened from baseline | 5 (4.1) | 8 (6.5) | 13 (5.3) |
| Clinically meaningful† worsened from baseline | 0 (0.0) | 1 (0.8) | 1 (0.4) |
| **Neutrophils Decreased** | | | |
| Improved from baseline | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Worsened from baseline | 5 (4.1) | 2 (1.6) | 7 (2.9) |
| Clinically meaningful† worsened from baseline | 3 (2.5) | 0 (0.0) | 3 (1.2) |
| **Phosphate Decreased** | | | |
| Improved from baseline | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Worsened from baseline | 27 (22.3) | 28 (22.8) | 55 (22.5) |
| Clinically meaningful† worsened from baseline | 27 (22.3) | 28 (22.8) | 55 (22.5) |
| **Platelet Decreased** | | | |
| Improved from baseline | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Worsened from baseline | 9 (7.4) | 13 (10.6) | 22 (9.0) |
| Clinically meaningful† worsened from baseline | 0 (0.0) | 1 (0.8) | 1 (0.4) |
| **Potassium Decreased** | | | |
| Improved from baseline | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Worsened from baseline | 11 (9.1) | 12 (9.8) | 23 (9.4) |
| Clinically meaningful† worsened from baseline | 1 (0.8) | 3 (2.4) | 4 (1.6) |
| **Potassium Increased** | | | |



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## 付録 2.7.4-123 臨床検査値の Grade がベースラインより悪化した患者の要約

### 001 試験パート B3（APaT 集団）（続き）

| Laboratory Test | MK-3475 10 mg/kg Q3W (N=121) | MK-3475 10 mg/kg Q2W (N=123) | Total (N=244) |
|---|---|---|---|
| **Potassium Increased** | | | |
| Improved from baseline | 0 (0.0) | 1 (0.8) | 1 (0.4) |
| Worsened from baseline | 11 (9.1) | 19 (15.4) | 30 (12.3) |
| Clinically meaningful† worsened from baseline | 5 (4.1) | 4 (3.3) | 9 (3.7) |
| **Prothrombin Intl. Normalized Ratio In** | | | |
| Improved from baseline | 0 (0.0) | 1 (0.8) | 1 (0.4) |
| Worsened from baseline | 6 (5.0) | 3 (2.4) | 9 (3.7) |
| Clinically meaningful† worsened from baseline | 4 (3.3) | 1 (0.8) | 5 (2.0) |
| **Sodium Decreased** | | | |
| Improved from baseline | 0 (0.0) | 1 (0.8) | 1 (0.4) |
| Worsened from baseline | 36 (29.8) | 42 (34.1) | 78 (32.0) |
| Clinically meaningful† worsened from baseline | 8 (6.6) | 9 (7.3) | 17 (7.0) |
| **Triglycerides** | | | |
| Improved from baseline | 2 (1.7) | 0 (0.0) | 2 (0.8) |
| Worsened from baseline | 30 (24.8) | 40 (32.5) | 70 (28.7) |
| Clinically meaningful† worsened from baseline | 4 (3.3) | 1 (0.8) | 5 (2.0) |

A missing baseline value was set to Grade 0.
† A clinically meaningful worsening in CTCAE grade was defined as a shift from less than Grade 3 to Grade 3 , 4 or 5 or a shift from Grade 0 to Grade 2.
(Database Cutoff Date: [redacted])

Data Source: [資料5.3.5.2.1.2: P001V02]



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## 付録 2.7.4-124 臨床検査値の Grade がベースラインより悪化した患者の要約

## 002 試験（APaT 集団）

| Laboratory Test | Control (N=171) | MK-3475 2 mg/kg Q3W (N=178) | MK-3475 10 mg/kg Q3W (N=179) |
|---|---|---|---|
| **Activated Partial Thromboplastin Time Increased** | | | |
| Improved from baseline | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Worsened from baseline | 10 (5.8) | 3 (1.7) | 3 (1.7) |
| Clinically meaningful[†] worsened from baseline | 1 (0.6) | 1 (0.6) | 2 (1.1) |
| **Alanine Aminotransferase Increased** | | | |
| Improved from baseline | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Worsened from baseline | 31 (18.1) | 34 (19.1) | 38 (21.2) |
| Clinically meaningful[†] worsened from baseline | 4 (2.3) | 5 (2.8) | 9 (5.0) |
| **Albumin Decreased** | | | |
| Improved from baseline | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Worsened from baseline | 67 (39.2) | 76 (42.7) | 81 (45.3) |
| Clinically meaningful[†] worsened from baseline | 22 (12.9) | 38 (21.3) | 34 (19.0) |
| **Alkaline Phosphatase Increased** | | | |
| Improved from baseline | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Worsened from baseline | 48 (28.1) | 63 (35.4) | 65 (36.3) |
| Clinically meaningful[†] worsened from baseline | 7 (4.1) | 11 (6.2) | 15 (8.4) |
| **Aspartate Aminotransferase Increased** | | | |
| Improved from baseline | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Worsened from baseline | 29 (17.0) | 46 (25.8) | 49 (27.4) |
| Clinically meaningful[†] worsened from baseline | 5 (2.9) | 9 (5.1) | 12 (6.7) |
| **Bicarbonate Decreased** | | | |



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## 付録 2.7.4-124 臨床検査値の Grade がベースラインより悪化した患者の要約

### 002 試験（APaT 集団）（続き）

| Laboratory Test | Control (N=171) | MK-3475 2 mg/kg Q3W (N=178) | MK-3475 10 mg/kg Q3W (N=179) |
|---|---|---|---|
| **Bicarbonate Decreased** | | | |
| Improved from baseline | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Worsened from baseline | 19 (11.1) | 34 (19.1) | 30 (16.8) |
| Clinically meaningful[†] worsened from baseline | 1 (0.6) | 1 (0.6) | 2 (1.1) |
| **Bilirubinn Increased** | | | |
| Improved from baseline | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Worsened from baseline | 14 (8.2) | 16 (9.0) | 16 (8.9) |
| Clinically meaningful[†] worsened from baseline | 7 (4.1) | 5 (2.8) | 6 (3.4) |
| **Calcium Decreased** | | | |
| Improved from baseline | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Worsened from baseline | 37 (21.6) | 46 (25.8) | 35 (19.6) |
| Clinically meaningful[†] worsened from baseline | 7 (4.1) | 15 (8.4) | 8 (4.5) |
| **Calcium Increased** | | | |
| Improved from baseline | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Worsened from baseline | 10 (5.8) | 14 (7.9) | 12 (6.7) |
| Clinically meaningful[†] worsened from baseline | 1 (0.6) | 1 (0.6) | 1 (0.6) |
| **Cholesterol** | | | |
| Improved from baseline | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Worsened from baseline | 46 (26.9) | 52 (29.2) | 75 (41.9) |
| Clinically meaningful[†] worsened from baseline | 4 (2.3) | 1 (0.6) | 4 (2.2) |
| **Creatinine Increased** | | | |



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## 付録 2.7.4-124 臨床検査値の Grade がベースラインより悪化した患者の要約
## 002 試験（APaT 集団）（続き）

| Laboratory Test | Control (N=171) | MK-3475 2 mg/kg Q3W (N=178) | MK-3475 10 mg/kg Q3W (N=179) |
|---|---|---|---|
| **Creatinine Increased** | | | |
| Improved from baseline | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Worsened from baseline | 26 (15.2) | 33 (18.5) | 36 (20.1) |
| Clinically meaningful[†] worsened from baseline | 5 (2.9) | 6 (3.4) | 5 (2.8) |
| **Gamma Glutamyl Transferase Increased** | | | |
| Improved from baseline | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Worsened from baseline | 2 (1.2) | 7 (3.9) | 4 (2.2) |
| Clinically meaningful[†] worsened from baseline | 1 (0.6) | 2 (1.1) | 3 (1.7) |
| **Glucose Decreased** | | | |
| Improved from baseline | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Worsened from baseline | 12 (7.0) | 13 (7.3) | 20 (11.2) |
| Clinically meaningful[†] worsened from baseline | 4 (2.3) | 2 (1.1) | 2 (1.1) |
| **Glucose Increased** | | | |
| Improved from baseline | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Worsened from baseline | 95 (55.6) | 113 (63.5) | 113 (63.1) |
| Clinically meaningful[†] worsened from baseline | 37 (21.6) | 46 (25.8) | 24 (13.4) |
| **Hemoglobin Decreased** | | | |
| Improved from baseline | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Worsened from baseline | 130 (76.0) | 123 (69.1) | 125 (69.8) |
| Clinically meaningful[†] worsened from baseline | 57 (33.3) | 54 (30.3) | 40 (22.3) |
| **Leukocytes Decreased** | | | |



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## 付録 2.7.4-124 臨床検査値の Grade がベースラインより悪化した患者の要約
## 002 試験（APaT 集団）（続き）

| Laboratory Test | Control (N=171) | MK-3475 2 mg/kg Q3W (N=178) | MK-3475 10 mg/kg Q3W (N=179) |
|---|---|---|---|
| **Leukocytes Decreased** | | | |
| Improved from baseline | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Worsened from baseline | 64 (37.4) | 20 (11.2) | 19 (10.6) |
| Clinically meaningful† worsened from baseline | 32 (18.7) | 5 (2.8) | 5 (2.8) |
| **Lymphocytes Decreased** | | | |
| Improved from baseline | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Worsened from baseline | 88 (51.5) | 92 (51.7) | 84 (46.9) |
| Clinically meaningful† worsened from baseline | 58 (33.9) | 45 (25.3) | 51 (28.5) |
| **Magnesium Decreased** | | | |
| Improved from baseline | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Worsened from baseline | 29 (17.0) | 33 (18.5) | 31 (17.3) |
| Clinically meaningful† worsened from baseline | 3 (1.8) | 2 (1.1) | 0 (0.0) |
| **Magnesium Increased** | | | |
| Improved from baseline | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Worsened from baseline | 4 (2.3) | 7 (3.9) | 5 (2.8) |
| Clinically meaningful† worsened from baseline | 1 (0.6) | 2 (1.1) | 0 (0.0) |
| **Neutrophils Decreased** | | | |
| Improved from baseline | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Worsened from baseline | 45 (26.3) | 14 (7.9) | 11 (6.1) |
| Clinically meaningful† worsened from baseline | 32 (18.7) | 8 (4.5) | 5 (2.8) |
| **Neutrophils Increased** | | | |



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## 付録 2.7.4-124 臨床検査値の Grade がベースラインより悪化した患者の要約
## 002 試験（APaT 集団）（続き）

| Laboratory Test | Control (N=171) | MK-3475 2 mg/kg Q3W (N=178) | MK-3475 10 mg/kg Q3W (N=179) |
|---|---|---|---|
| **Neutrophils Increased** | | | |
| Improved from baseline | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Worsened from baseline | 2 (1.2) | 0 (0.0) | 0 (0.0) |
| Clinically meaningful[†] worsened from baseline | 2 (1.2) | 0 (0.0) | 0 (0.0) |
| **Phosphate Decreased** | | | |
| Improved from baseline | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Worsened from baseline | 26 (15.2) | 25 (14.0) | 31 (17.3) |
| Clinically meaningful[†] worsened from baseline | 23 (13.5) | 22 (12.4) | 24 (13.4) |
| **Platelet Decreased** | | | |
| Improved from baseline | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Worsened from baseline | 65 (38.0) | 24 (13.5) | 16 (8.9) |
| Clinically meaningful[†] worsened from baseline | 21 (12.3) | 3 (1.7) | 4 (2.2) |
| **Platelet Increased** | | | |
| Improved from baseline | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Worsened from baseline | 1 (0.6) | 0 (0.0) | 0 (0.0) |
| Clinically meaningful[†] worsened from baseline | 1 (0.6) | 0 (0.0) | 0 (0.0) |
| **Potassium Decreased** | | | |
| Improved from baseline | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Worsened from baseline | 22 (12.9) | 22 (12.4) | 23 (12.8) |
| Clinically meaningful[†] worsened from baseline | 3 (1.8) | 4 (2.2) | 3 (1.7) |
| **Potassium Increased** | | | |



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## 付録 2.7.4-124 臨床検査値の Grade がベースラインより悪化した患者の要約
## 002 試験（APaT 集団）（続き）

| Laboratory Test | Control (N=171) | MK-3475 2 mg/kg Q3W (N=178) | MK-3475 10 mg/kg Q3W (N=179) |
|---|---|---|---|
| **Potassium Increased** | | | |
| Improved from baseline | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Worsened from baseline | 16 (9.4) | 29 (16.3) | 25 (14.0) |
| Clinically meaningful† worsened from baseline | 3 (1.8) | 7 (3.9) | 8 (4.5) |
| **Prothrombin Intl. Normalized Ratio Increased** | | | |
| Improved from baseline | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Worsened from baseline | 7 (4.1) | 9 (5.1) | 3 (1.7) |
| Clinically meaningful† worsened from baseline | 1 (0.6) | 6 (3.4) | 2 (1.1) |
| **Sodium Decreased** | | | |
| Improved from baseline | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Worsened from baseline | 50 (29.2) | 80 (44.9) | 81 (45.3) |
| Clinically meaningful† worsened from baseline | 9 (5.3) | 15 (8.4) | 14 (7.8) |
| **Triglycerides** | | | |
| Improved from baseline | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Worsened from baseline | 73 (42.7) | 76 (42.7) | 92 (51.4) |
| Clinically meaningful† worsened from baseline | 11 (6.4) | 6 (3.4) | 9 (5.0) |

A missing baseline value was set to Grade 0.
† A clinically meaningful worsening in CTCAE grade was defined as a shift from less than Grade 3 to Grade 3 , 4 or 5 or a shift from Grade 0 to Grade 2.
(Database Cutoff Date: 12MAY2014).

Data Source: [資料5.3.5.1.1: P002V01]



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## 付録 2.7.4-125 臨床検査値の Grade がベースラインより悪化した患者での臨床検査値異常の最大 Grade の要約
## 002 試験（APaT 集団）

| Laboratory Test | Control (N=171) | MK-3475 2 mg/kg Q3W (N=178) | MK-3475 10 mg/kg Q3W (N=179) |
|---|---|---|---|
| **Activated Partial Thromboplastin Time Increased** | | | |
| Toxicity Grade 1 | 9 ( 5.3) | 2 ( 1.1) | 1 ( 0.6) |
| Toxicity Grade 2 | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) |
| Toxicity Grade 3 | 1 ( 0.6) | 1 ( 0.6) | 2 ( 1.1) |
| Toxicity Grade 4 | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) |
| **Alanine Aminotransferase Increased** | | | |
| Toxicity Grade 1 | 27 (15.8) | 29 (16.3) | 29 (16.2) |
| Toxicity Grade 2 | 3 ( 1.8) | 3 ( 1.7) | 6 ( 3.4) |
| Toxicity Grade 3 | 1 ( 0.6) | 2 ( 1.1) | 2 ( 1.1) |
| Toxicity Grade 4 | 0 ( 0.0) | 0 ( 0.0) | 1 ( 0.6) |
| **Albumin Decreased** | | | |
| Toxicity Grade 1 | 45 (26.3) | 38 (21.3) | 47 (26.3) |
| Toxicity Grade 2 | 21 (12.3) | 30 (16.9) | 33 (18.4) |
| Toxicity Grade 3 | 1 ( 0.6) | 8 ( 4.5) | 1 ( 0.6) |
| Toxicity Grade 4 | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) |
| **Alkaline Phosphatase Increased** | | | |
| Toxicity Grade 1 | 41 (24.0) | 52 (29.2) | 50 (27.9) |
| Toxicity Grade 2 | 4 ( 2.3) | 4 ( 2.2) | 11 ( 6.1) |
| Toxicity Grade 3 | 3 ( 1.8) | 7 ( 3.9) | 3 ( 1.7) |
| Toxicity Grade 4 | 0 ( 0.0) | 0 ( 0.0) | 1 ( 0.6) |
| **Aspartate Aminotransferase Increased** | | | |
| Toxicity Grade 1 | 24 (14.0) | 37 (20.8) | 37 (20.7) |
| Toxicity Grade 2 | 4 ( 2.3) | 6 ( 3.4) | 7 ( 3.9) |
| Toxicity Grade 3 | 0 ( 0.0) | 2 ( 1.1) | 3 ( 1.7) |
| Toxicity Grade 4 | 1 ( 0.6) | 1 ( 0.6) | 2 ( 1.1) |



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## 付録 2.7.4-125 臨床検査値の Grade がベースラインより悪化した患者での臨床検査値異常の最大 Grade の要約
## 002 試験（APaT 集団）（続き）

| Laboratory Test | Control (N=171) | MK-3475 2 mg/kg Q3W (N=178) | MK-3475 10 mg/kg Q3W (N=179) |
|---|---|---|---|
| **Bicarbonate Decreased** | | | |
| Toxicity Grade 1 | 18 (10.5) | 33 (18.5) | 28 (15.6) |
| Toxicity Grade 2 | 1 ( 0.6) | 1 ( 0.6) | 1 ( 0.6) |
| Toxicity Grade 3 | 0 ( 0.0) | 0 ( 0.0) | 1 ( 0.6) |
| Toxicity Grade 4 | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) |
| **Bilirubinn Increased** | | | |
| Toxicity Grade 1 | 7 ( 4.1) | 11 ( 6.2) | 10 ( 5.6) |
| Toxicity Grade 2 | 5 ( 2.9) | 3 ( 1.7) | 2 ( 1.1) |
| Toxicity Grade 3 | 1 ( 0.6) | 0 ( 0.0) | 4 ( 2.2) |
| Toxicity Grade 4 | 1 ( 0.6) | 2 ( 1.1) | 0 ( 0.0) |
| **Calcium Decreased** | | | |
| Toxicity Grade 1 | 30 (17.5) | 31 (17.4) | 27 (15.1) |
| Toxicity Grade 2 | 4 ( 2.3) | 13 ( 7.3) | 8 ( 4.5) |
| Toxicity Grade 3 | 1 ( 0.6) | 1 ( 0.6) | 0 ( 0.0) |
| Toxicity Grade 4 | 2 ( 1.2) | 1 ( 0.6) | 0 ( 0.0) |
| **Calcium Increased** | | | |
| Toxicity Grade 1 | 9 ( 5.3) | 13 ( 7.3) | 11 ( 6.1) |
| Toxicity Grade 2 | 0 ( 0.0) | 0 ( 0.0) | 1 ( 0.6) |
| Toxicity Grade 3 | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) |
| Toxicity Grade 4 | 1 ( 0.6) | 1 ( 0.6) | 0 ( 0.0) |
| **Cholesterol** | | | |
| Toxicity Grade 1 | 42 (24.6) | 51 (28.7) | 71 (39.7) |
| Toxicity Grade 2 | 4 ( 2.3) | 1 ( 0.6) | 3 ( 1.7) |
| Toxicity Grade 3 | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) |
| Toxicity Grade 4 | 0 ( 0.0) | 0 ( 0.0) | 1 ( 0.6) |



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## 付録 2.7.4-125 臨床検査値の Grade がベースラインより悪化した患者での臨床検査値異常の最大 Grade の要約
## 002 試験（APaT 集団）（続き）

| Laboratory Test | Control (N=171) | MK-3475 2 mg/kg Q3W (N=178) | MK-3475 10 mg/kg Q3W (N=179) |
|---|---|---|---|
| **Creatine Kinase** | | | |
| Toxicity Grade 1 | 1 ( 0.6) | 1 ( 0.6) | 1 ( 0.6) |
| Toxicity Grade 2 | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) |
| Toxicity Grade 3 | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) |
| Toxicity Grade 4 | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) |
| **Creatinine Increased** | | | |
| Toxicity Grade 1 | 21 (12.3) | 27 (15.2) | 31 (17.3) |
| Toxicity Grade 2 | 3 ( 1.8) | 4 ( 2.2) | 5 ( 2.8) |
| Toxicity Grade 3 | 2 ( 1.2) | 2 ( 1.1) | 0 ( 0.0) |
| Toxicity Grade 4 | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) |
| **Gamma Glutamyl Transferase Increased** | | | |
| Toxicity Grade 1 | 1 ( 0.6) | 5 ( 2.8) | 1 ( 0.6) |
| Toxicity Grade 2 | 0 ( 0.0) | 1 ( 0.6) | 0 ( 0.0) |
| Toxicity Grade 3 | 1 ( 0.6) | 1 ( 0.6) | 2 ( 1.1) |
| Toxicity Grade 4 | 0 ( 0.0) | 0 ( 0.0) | 1 ( 0.6) |
| **Glucose Decreased** | | | |
| Toxicity Grade 1 | 8 ( 4.7) | 11 ( 6.2) | 18 (10.1) |
| Toxicity Grade 2 | 2 ( 1.2) | 1 ( 0.6) | 1 ( 0.6) |
| Toxicity Grade 3 | 1 ( 0.6) | 1 ( 0.6) | 0 ( 0.0) |
| Toxicity Grade 4 | 1 ( 0.6) | 0 ( 0.0) | 1 ( 0.6) |
| **Glucose Increased** | | | |
| Toxicity Grade 1 | 58 (33.9) | 67 (37.6) | 89 (49.7) |
| Toxicity Grade 2 | 27 (15.8) | 30 (16.9) | 15 ( 8.4) |
| Toxicity Grade 3 | 10 ( 5.8) | 16 ( 9.0) | 8 ( 4.5) |
| Toxicity Grade 4 | 0 ( 0.0) | 0 ( 0.0) | 1 ( 0.6) |



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## 付録 2.7.4-125 臨床検査値の Grade がベースラインより悪化した患者での臨床検査値異常の最大 Grade の要約
## 002 試験（APaT 集団）（続き）

| Laboratory Test | Control (N=171) | MK-3475 2 mg/kg Q3W (N=178) | MK-3475 10 mg/kg Q3W (N=179) |
|---|---|---|---|
| **Hemoglobin Decreased** | | | |
| Toxicity Grade 1 | 73 (42.7) | 69 (38.8) | 85 (47.5) |
| Toxicity Grade 2 | 43 (25.1) | 32 (18.0) | 32 (17.9) |
| Toxicity Grade 3 | 9 ( 5.3) | 17 ( 9.6) | 7 ( 3.9) |
| Toxicity Grade 4 | 5 ( 2.9) | 5 ( 2.8) | 1 ( 0.6) |
| **Leukocytes Decreased** | | | |
| Toxicity Grade 1 | 32 (18.7) | 15 ( 8.4) | 14 ( 7.8) |
| Toxicity Grade 2 | 14 ( 8.2) | 5 ( 2.8) | 4 ( 2.2) |
| Toxicity Grade 3 | 12 ( 7.0) | 0 ( 0.0) | 1 ( 0.6) |
| Toxicity Grade 4 | 6 ( 3.5) | 0 ( 0.0) | 0 ( 0.0) |
| **Lymphocytes Decreased** | | | |
| Toxicity Grade 1 | 30 (17.5) | 47 (26.4) | 33 (18.4) |
| Toxicity Grade 2 | 39 (22.8) | 33 (18.5) | 33 (18.4) |
| Toxicity Grade 3 | 17 ( 9.9) | 10 ( 5.6) | 17 ( 9.5) |
| Toxicity Grade 4 | 2 ( 1.2) | 2 ( 1.1) | 1 ( 0.6) |
| **Magnesium Decreased** | | | |
| Toxicity Grade 1 | 26 (15.2) | 31 (17.4) | 31 (17.3) |
| Toxicity Grade 2 | 2 ( 1.2) | 2 ( 1.1) | 0 ( 0.0) |
| Toxicity Grade 3 | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) |
| Toxicity Grade 4 | 1 ( 0.6) | 0 ( 0.0) | 0 ( 0.0) |
| **Magnesium Increased** | | | |
| Toxicity Grade 1 | 3 ( 1.8) | 5 ( 2.8) | 5 ( 2.8) |
| Toxicity Grade 2 | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) |
| Toxicity Grade 3 | 1 ( 0.6) | 2 ( 1.1) | 0 ( 0.0) |
| Toxicity Grade 4 | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) |



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## 付録 2.7.4-125 臨床検査値の Grade がベースラインより悪化した患者での臨床検査値異常の最大 Grade の要約
## 002 試験（APaT 集団）（続き）

| Laboratory Test | Control (N=171) | MK-3475 2 mg/kg Q3W (N=178) | MK-3475 10 mg/kg Q3W (N=179) |
|---|---|---|---|
| **Neutrophils Decreased** | | | |
| Toxicity Grade 1 | 13 ( 7.6) | 6 ( 3.4) | 6 ( 3.4) |
| Toxicity Grade 2 | 15 ( 8.8) | 4 ( 2.2) | 2 ( 1.1) |
| Toxicity Grade 3 | 10 ( 5.8) | 1 ( 0.6) | 1 ( 0.6) |
| Toxicity Grade 4 | 7 ( 4.1) | 3 ( 1.7) | 2 ( 1.1) |
| **Neutrophils Increased** | | | |
| Toxicity Grade 1 | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) |
| Toxicity Grade 2 | 1 ( 0.6) | 0 ( 0.0) | 0 ( 0.0) |
| Toxicity Grade 3 | 1 ( 0.6) | 0 ( 0.0) | 0 ( 0.0) |
| Toxicity Grade 4 | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) |
| **Phosphate Decreased** | | | |
| Toxicity Grade 1 | 3 ( 1.8) | 3 ( 1.7) | 7 ( 3.9) |
| Toxicity Grade 2 | 20 (11.7) | 16 ( 9.0) | 18 (10.1) |
| Toxicity Grade 3 | 3 ( 1.8) | 6 ( 3.4) | 6 ( 3.4) |
| Toxicity Grade 4 | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) |
| **Platelet Decreased** | | | |
| Toxicity Grade 1 | 44 (25.7) | 21 (11.8) | 12 ( 6.7) |
| Toxicity Grade 2 | 9 ( 5.3) | 1 ( 0.6) | 3 ( 1.7) |
| Toxicity Grade 3 | 8 ( 4.7) | 2 ( 1.1) | 1 ( 0.6) |
| Toxicity Grade 4 | 4 ( 2.3) | 0 ( 0.0) | 0 ( 0.0) |
| **Platelet Increased** | | | |
| Toxicity Grade 1 | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) |
| Toxicity Grade 2 | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) |
| Toxicity Grade 3 | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) |
| Toxicity Grade 4 | 1 ( 0.6) | 0 ( 0.0) | 0 ( 0.0) |



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## 付録 2.7.4-125 臨床検査値の Grade がベースラインより悪化した患者での臨床検査値異常の最大 Grade の要約
## 002 試験（APaT 集団）（続き）

| Laboratory Test | Control (N=171) | MK-3475 2 mg/kg Q3W (N=178) | MK-3475 10 mg/kg Q3W (N=179) |
|---|---|---|---|
| **Potassium Decreased** | | | |
| Toxicity Grade 1 | 19 (11.1) | 18 (10.1) | 20 (11.2) |
| Toxicity Grade 2 | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) |
| Toxicity Grade 3 | 3 ( 1.8) | 4 ( 2.2) | 3 ( 1.7) |
| Toxicity Grade 4 | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) |
| **Potassium Increased** | | | |
| Toxicity Grade 1 | 13 ( 7.6) | 22 (12.4) | 17 ( 9.5) |
| Toxicity Grade 2 | 2 ( 1.2) | 6 ( 3.4) | 6 ( 3.4) |
| Toxicity Grade 3 | 0 ( 0.0) | 0 ( 0.0) | 1 ( 0.6) |
| Toxicity Grade 4 | 1 ( 0.6) | 1 ( 0.6) | 1 ( 0.6) |
| **Prothrombin Intl. Normalized Ratio Increased** | | | |
| Toxicity Grade 1 | 6 ( 3.5) | 3 ( 1.7) | 1 ( 0.6) |
| Toxicity Grade 2 | 0 ( 0.0) | 2 ( 1.1) | 0 ( 0.0) |
| Toxicity Grade 3 | 1 ( 0.6) | 4 ( 2.2) | 2 ( 1.1) |
| Toxicity Grade 4 | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) |
| **Sodium Decreased** | | | |
| Toxicity Grade 1 | 41 (24.0) | 65 (36.5) | 67 (37.4) |
| Toxicity Grade 2 | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) |
| Toxicity Grade 3 | 7 ( 4.1) | 13 ( 7.3) | 13 ( 7.3) |
| Toxicity Grade 4 | 2 ( 1.2) | 2 ( 1.1) | 1 ( 0.6) |
| **Sodium Increased** | | | |
| Toxicity Grade 1 | 9 ( 5.3) | 5 ( 2.8) | 9 ( 5.0) |
| Toxicity Grade 2 | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) |
| Toxicity Grade 3 | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) |
| Toxicity Grade 4 | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) |



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## 付録 2.7.4-125 臨床検査値の Grade がベースラインより悪化した患者での臨床検査値異常の最大 Grade の要約
## 002 試験（APaT 集団）（続き）

| Laboratory Test | Control (N=171) | MK-3475 2 mg/kg Q3W (N=178) | MK-3475 10 mg/kg Q3W (N=179) |
|---|---|---|---|
| **Triglycerides** | | | |
| Toxicity Grade 1 | 62 (36.3) | 70 (39.3) | 83 (46.4) |
| Toxicity Grade 2 | 10 ( 5.8) | 6 ( 3.4) | 9 ( 5.0) |
| Toxicity Grade 3 | 1 ( 0.6) | 0 ( 0.0) | 0 ( 0.0) |
| Toxicity Grade 4 | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) |
| If a patient had more than one graded abnormalities for a lab test, only the hightest grade is counted.<br>Grades are based on NCI CTCAE version 3.<br>(Database Cutoff Date: 12MAY2014). | | | |

Data Source: [資料5.3.5.1.1: P002V01]



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## 付録 2.7.4-126 臨床検査値の Grade がベースラインより悪化した患者の要約

### 006 試験（APaT 集団）

| Laboratory Test | Control (N=256) | MK-3475 10 mg/kg Q2W (N=278) | MK-3475 10 mg/kg Q3W (N=277) |
|---|---|---|---|
| **APTT Increased** | | | |
| Improved from baseline | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Worsened from baseline | 2 (0.8) | 6 (2.2) | 5 (1.8) |
| Clinically meaningful† worsened from baseline | 1 (0.4) | 6 (2.2) | 5 (1.8) |
| **Alanine Aminotransferase Increased** | | | |
| Improved from baseline | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Worsened from baseline | 43 (16.8) | 84 (30.2) | 56 (20.2) |
| Clinically meaningful† worsened from baseline | 3 (1.2) | 13 (4.7) | 2 (0.7) |
| **Albumin Decreased** | | | |
| Improved from baseline | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Worsened from baseline | 59 (23.0) | 80 (28.8) | 67 (24.2) |
| Clinically meaningful† worsened from baseline | 14 (5.5) | 28 (10.1) | 26 (9.4) |
| **Alkaline Phosphatase Increased** | | | |
| Improved from baseline | 0 (0.0) | 0 (0.0) | 0 (0.0) |



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## 付録 2.7.4-126 臨床検査値の Grade がベースラインより悪化した患者の要約

### 006 試験（APaT 集団）（続き）

| Laboratory Test | Control (N=256) | MK-3475 10 mg/kg Q2W (N=278) | MK-3475 10 mg/kg Q3W (N=277) |
|---|---|---|---|
| **Alkaline Phosphatase Increased** | | | |
| Worsened from baseline | 51 (19.9) | 70 (25.2) | 62 (22.4) |
| Clinically meaningful† worsened from baseline | 10 (3.9) | 9 (3.2) | 12 (4.3) |
| **Amylase Increased** | | | |
| Improved from baseline | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Worsened from baseline | 0 (0.0) | 1 (0.4) | 0 (0.0) |
| Clinically meaningful† worsened from baseline | 0 (0.0) | 1 (0.4) | 0 (0.0) |
| **Aspartate Aminotransferase Increased** | | | |
| Improved from baseline | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Worsened from baseline | 48 (18.8) | 86 (30.9) | 65 (23.5) |
| Clinically meaningful† worsened from baseline | 3 (1.2) | 11 (4.0) | 6 (2.2) |
| **Bilirubinn Increased** | | | |
| Improved from baseline | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Worsened from baseline | 15 (5.9) | 39 (14.0) | 23 (8.3) |



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## 付録 2.7.4-126 臨床検査値の Grade がベースラインより悪化した患者の要約

### 006 試験（APaT 集団）（続き）

| Laboratory Test | Control (N=256) | MK-3475 10 mg/kg Q2W (N=278) | MK-3475 10 mg/kg Q3W (N=277) |
|---|---|---|---|
| **Bilirubinn Increased** | | | |
| Clinically meaningful† worsened from baseline | 6 (2.3) | 10 (3.6) | 7 (2.5) |
| **Calcium Decreased** | | | |
| Improved from baseline | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Worsened from baseline | 22 (8.6) | 59 (21.2) | 52 (18.8) |
| Clinically meaningful† worsened from baseline | 2 (0.8) | 10 (3.6) | 10 (3.6) |
| **Calcium Increased** | | | |
| Improved from baseline | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Worsened from baseline | 11 (4.3) | 18 (6.5) | 17 (6.1) |
| Clinically meaningful† worsened from baseline | 2 (0.8) | 4 (1.4) | 4 (1.4) |
| **Cholesterol** | | | |
| Improved from baseline | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Worsened from baseline | 67 (26.2) | 128 (46.0) | 102 (36.8) |
| Clinically meaningful† worsened from baseline | 3 (1.2) | 11 (4.0) | 13 (4.7) |



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## 付録 2.7.4-126 臨床検査値の Grade がベースラインより悪化した患者の要約

### 006 試験（APaT 集団）（続き）

| Laboratory Test | Control (N=256) | MK-3475 10 mg/kg Q2W (N=278) | MK-3475 10 mg/kg Q3W (N=277) |
|---|---|---|---|
| **Creatinine Increased** | | | |
| Improved from baseline | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Worsened from baseline | 32 (12.5) | 50 (18.0) | 42 (15.2) |
| Clinically meaningful† worsened from baseline | 6 (2.3) | 6 (2.2) | 2 (0.7) |
| **Gamma Glutamyl Transferase Increased** | | | |
| Improved from baseline | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Worsened from baseline | 3 (1.2) | 2 (0.7) | 1 (0.4) |
| Clinically meaningful† worsened from baseline | 3 (1.2) | 1 (0.4) | 0 (0.0) |
| **Glucose Decreased** | | | |
| Improved from baseline | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Worsened from baseline | 5 (2.0) | 22 (7.9) | 13 (4.7) |
| Clinically meaningful† worsened from baseline | 0 (0.0) | 2 (0.7) | 0 (0.0) |
| **Glucose Increased** | | | |
| Improved from baseline | 0 (0.0) | 0 (0.0) | 0 (0.0) |



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## 付録 2.7.4-126 臨床検査値の Grade がベースラインより悪化した患者の要約

### 006 試験（APaT 集団）（続き）

| Laboratory Test | Control (N=256) | MK-3475 10 mg/kg Q2W (N=278) | MK-3475 10 mg/kg Q3W (N=277) |
|---|---|---|---|
| **Glucose Increased** | | | |
| Worsened from baseline | 116 (45.3) | 164 (59.0) | 152 (54.9) |
| Clinically meaningful† worsened from baseline | 34 (13.3) | 46 (16.5) | 31 (11.2) |
| **Hemoglobin Decreased** | | | |
| Improved from baseline | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Worsened from baseline | 106 (41.4) | 133 (47.8) | 130 (46.9) |
| Clinically meaningful† worsened from baseline | 24 (9.4) | 34 (12.2) | 27 (9.7) |
| **Leukocytes Decreased** | | | |
| Improved from baseline | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Worsened from baseline | 14 (5.5) | 44 (15.8) | 32 (11.6) |
| Clinically meaningful† worsened from baseline | 2 (0.8) | 9 (3.2) | 3 (1.1) |
| **Lymphocytes Decreased** | | | |
| Improved from baseline | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Worsened from baseline | 59 (23.0) | 120 (43.2) | 111 (40.1) |



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## 付録 2.7.4-126 臨床検査値の Grade がベースラインより悪化した患者の要約

### 006 試験（APaT 集団）（続き）

| Laboratory Test | Control (N=256) | MK-3475 10 mg/kg Q2W (N=278) | MK-3475 10 mg/kg Q3W (N=277) |
|---|---|---|---|
| **Lymphocytes Decreased** | | | |
| Clinically meaningful† worsened from baseline | 25 (9.8) | 58 (20.9) | 51 (18.4) |
| **Magnesium Decreased** | | | |
| Improved from baseline | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Worsened from baseline | 30 (11.7) | 41 (14.7) | 39 (14.1) |
| Clinically meaningful† worsened from baseline | 4 (1.6) | 8 (2.9) | 3 (1.1) |
| **Magnesium Increased** | | | |
| Improved from baseline | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Worsened from baseline | 8 (3.1) | 15 (5.4) | 23 (8.3) |
| Clinically meaningful† worsened from baseline | 0 (0.0) | 4 (1.4) | 1 (0.4) |
| **Neutrophils Decreased** | | | |
| Improved from baseline | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Worsened from baseline | 13 (5.1) | 35 (12.6) | 18 (6.5) |
| Clinically meaningful† worsened from baseline | 3 (1.2) | 15 (5.4) | 8 (2.9) |



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## 付録 2.7.4-126 臨床検査値の Grade がベースラインより悪化した患者の要約

### 006 試験（APaT 集団）（続き）

| Laboratory Test | Control (N=256) | MK-3475 10 mg/kg Q2W (N=278) | MK-3475 10 mg/kg Q3W (N=277) |
|---|---|---|---|
| **Phosphate Decreased** | | | |
| Improved from baseline | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Worsened from baseline | 23 (9.0) | 48 (17.3) | 56 (20.2) |
| Clinically meaningful† worsened from baseline | 19 (7.4) | 39 (14.0) | 47 (17.0) |
| **Platelet Decreased** | | | |
| Improved from baseline | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Worsened from baseline | 9 (3.5) | 37 (13.3) | 32 (11.6) |
| Clinically meaningful† worsened from baseline | 1 (0.4) | 4 (1.4) | 2 (0.7) |
| **Potassium Decreased** | | | |
| Improved from baseline | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Worsened from baseline | 21 (8.2) | 42 (15.1) | 27 (9.7) |
| Clinically meaningful† worsened from baseline | 4 (1.6) | 5 (1.8) | 3 (1.1) |
| **Potassium Increased** | | | |
| Improved from baseline | 0 (0.0) | 0 (0.0) | 0 (0.0) |



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## 付録 2.7.4-126 臨床検査値の Grade がベースラインより悪化した患者の要約

### 006 試験（APaT 集団）（続き）

| Laboratory Test | Control (N=256) | MK-3475 10 mg/kg Q2W (N=278) | MK-3475 10 mg/kg Q3W (N=277) |
|---|---|---|---|
| **Potassium Increased** | | | |
| Worsened from baseline | 13 (5.1) | 39 (14.0) | 34 (12.3) |
| Clinically meaningful† worsened from baseline | 4 (1.6) | 7 (2.5) | 10 (3.6) |
| **Prothrombin Intl. Normalized Ratio Incre** | | | |
| Improved from baseline | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Worsened from baseline | 0 (0.0) | 2 (0.7) | 1 (0.4) |
| Clinically meaningful† worsened from baseline | 0 (0.0) | 1 (0.4) | 0 (0.0) |
| **Sodium Decreased** | | | |
| Improved from baseline | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Worsened from baseline | 45 (17.6) | 78 (28.1) | 70 (25.3) |
| Clinically meaningful† worsened from baseline | 7 (2.7) | 7 (2.5) | 10 (3.6) |
| **Sodium Increased** | | | |
| Improved from baseline | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Worsened from baseline | 7 (2.7) | 27 (9.7) | 21 (7.6) |



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### 006 試験（APaT 集団）（続き）

| Laboratory Test | Control (N=256) | MK-3475 10 mg/kg Q2W (N=278) | MK-3475 10 mg/kg Q3W (N=277) |
|---|---|---|---|
| **Sodium Increased** | | | |
| Clinically meaningful† worsened from baseline | 0 (0.0) | 2 (0.7) | 0 (0.0) |
| **Triacylglycerol Lipase Increased** | | | |
| Improved from baseline | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Worsened from baseline | 0 (0.0) | 0 (0.0) | 1 (0.4) |
| Clinically meaningful† worsened from baseline | 0 (0.0) | 0 (0.0) | 1 (0.4) |
| **Triglycerides** | | | |
| Improved from baseline | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Worsened from baseline | 108 (42.2) | 161 (57.9) | 149 (53.8) |
| Clinically meaningful† worsened from baseline | 18 (7.0) | 36 (12.9) | 36 (13.0) |

A missing baseline value was set to Grade 0.
† A clinically meaningful worsening in CTCAE grade was defined as a shift from less than Grade 3 to Grade 3 , 4 or 5 or a shift from Grade 0 to Grade 2.
(Database Cutoff Date: 03SEP2014)

Data Source: [資料5.3.5.1.2: P006V01]



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## 付録 2.7.4-127 臨床検査値の Grade がベースラインより悪化した患者での臨床検査値異常の最大 Grade の要約
## 006 試験（APaT 集団）

| Laboratory Test | Control (N=256) | MK-3475 10 mg/kg Q2W (N=278) | MK-3475 10 mg/kg Q3W (N=277) | MK-3475 combined (N=555) |
|---|---|---|---|---|
| **APTT Decreased** | | | | |
| Toxicity Grade 1 | 0 ( 0.0) | 3 ( 1.1) | 2 ( 0.7) | 5 ( 0.9) |
| Toxicity Grade 2 | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) |
| Toxicity Grade 3 | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) |
| Toxicity Grade 4 | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) |
| **APTT Increased** | | | | |
| Toxicity Grade 1 | 1 ( 0.4) | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) |
| Toxicity Grade 2 | 0 ( 0.0) | 1 ( 0.4) | 1 ( 0.4) | 2 ( 0.4) |
| Toxicity Grade 3 | 1 ( 0.4) | 5 ( 1.8) | 4 ( 1.4) | 9 ( 1.6) |
| Toxicity Grade 4 | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) |
| **Alanine Aminotransferase Increased** | | | | |
| Toxicity Grade 1 | 40 (15.6) | 71 (25.5) | 54 (19.5) | 125 (22.5 |
| Toxicity Grade 2 | 1 ( 0.4) | 7 ( 2.5) | 0 ( 0.0) | 7 ( 1.3) |
| Toxicity Grade 3 | 2 ( 0.8) | 5 ( 1.8) | 2 ( 0.7) | 7 ( 1.3) |
| Toxicity Grade 4 | 0 ( 0.0) | 1 ( 0.4) | 0 ( 0.0) | 1 ( 0.2) |
| **Albumin Decreased** | | | | |
| Toxicity Grade 1 | 45 (17.6) | 52 (18.7) | 41 (14.8) | 93 (16.8) |
| Toxicity Grade 2 | 13 ( 5.1) | 24 ( 8.6) | 21 ( 7.6) | 45 ( 8.1) |
| Toxicity Grade 3 | 1 ( 0.4) | 4 ( 1.4) | 5 ( 1.8) | 9 ( 1.6) |
| Toxicity Grade 4 | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) |
| **Alkaline Phosphatase Increased** | | | | |
| Toxicity Grade 1 | 41 (16.0) | 61 (21.9) | 50 (18.1) | 111 (20.0 |
| Toxicity Grade 2 | 10 ( 3.9) | 8 ( 2.9) | 6 ( 2.2) | 14 ( 2.5) |
| Toxicity Grade 3 | 0 ( 0.0) | 1 ( 0.4) | 6 ( 2.2) | 7 ( 1.3) |
| Toxicity Grade 4 | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) |



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## 付録 2.7.4-127 臨床検査値の Grade がベースラインより悪化した患者での臨床検査値異常の最大 Grade の要約
## 006 試験（APaT 集団）（続き）

| Laboratory Test | Control (N=256) | MK-3475 10 mg/kg Q2W (N=278) | MK-3475 10 mg/kg Q3W (N=277) | MK-3475 combined (N=555) |
|---|---|---|---|---|
| **Amylase Increased** | | | | |
| Toxicity Grade 1 | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) |
| Toxicity Grade 2 | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) |
| Toxicity Grade 3 | 0 ( 0.0) | 1 ( 0.4) | 0 ( 0.0) | 1 ( 0.2) |
| Toxicity Grade 4 | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) |
| **Aspartate Aminotransferase Increased** | | | | |
| Toxicity Grade 1 | 45 (17.6) | 75 (27.0) | 59 (21.3) | 134 (24.1 |
| Toxicity Grade 2 | 3 ( 1.2) | 8 ( 2.9) | 4 ( 1.4) | 12 ( 2.2) |
| Toxicity Grade 3 | 0 ( 0.0) | 3 ( 1.1) | 2 ( 0.7) | 5 ( 0.9) |
| Toxicity Grade 4 | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) |
| **Bilirubinn Increased** | | | | |
| Toxicity Grade 1 | 9 ( 3.5) | 29 (10.4) | 16 ( 5.8) | 45 ( 8.1) |
| Toxicity Grade 2 | 5 ( 2.0) | 9 ( 3.2) | 6 ( 2.2) | 15 ( 2.7) |
| Toxicity Grade 3 | 1 ( 0.4) | 1 ( 0.4) | 1 ( 0.4) | 2 ( 0.4) |
| Toxicity Grade 4 | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) |
| **Calcium Decreased** | | | | |
| Toxicity Grade 1 | 20 ( 7.8) | 49 (17.6) | 42 (15.2) | 91 (16.4) |
| Toxicity Grade 2 | 2 ( 0.8) | 5 ( 1.8) | 8 ( 2.9) | 13 ( 2.3) |
| Toxicity Grade 3 | 0 ( 0.0) | 2 ( 0.7) | 2 ( 0.7) | 4 ( 0.7) |
| Toxicity Grade 4 | 0 ( 0.0) | 3 ( 1.1) | 0 ( 0.0) | 3 ( 0.5) |
| **Calcium Increased** | | | | |
| Toxicity Grade 1 | 9 ( 3.5) | 14 ( 5.0) | 13 ( 4.7) | 27 ( 4.9) |
| Toxicity Grade 2 | 2 ( 0.8) | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) |
| Toxicity Grade 3 | 0 ( 0.0) | 0 ( 0.0) | 1 ( 0.4) | 1 ( 0.2) |
| Toxicity Grade 4 | 0 ( 0.0) | 4 ( 1.4) | 3 ( 1.1) | 7 ( 1.3) |



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## 付録 2.7.4-127 臨床検査値の Grade がベースラインより悪化した患者での臨床検査値異常の最大 Grade の要約
## 006 試験（APaT 集団）（続き）

| Laboratory Test | Control (N=256) | MK-3475 10 mg/kg Q2W (N=278) | MK-3475 10 mg/kg Q3W (N=277) | MK-3475 combined (N=555) |
|---|---|---|---|---|
| **Cholesterol** | | | | |
| Toxicity Grade 1 | 64 (25.0) | 117 (42.1 | 89 (32.1) | 206 (37.1 |
| Toxicity Grade 2 | 3 ( 1.2) | 8 ( 2.9) | 10 ( 3.6) | 18 ( 3.2) |
| Toxicity Grade 3 | 0 ( 0.0) | 1 ( 0.4) | 0 ( 0.0) | 1 ( 0.2) |
| Toxicity Grade 4 | 0 ( 0.0) | 2 ( 0.7) | 3 ( 1.1) | 5 ( 0.9) |
| **Creatine Kinase** | | | | |
| Toxicity Grade 1 | 0 ( 0.0) | 0 ( 0.0) | 2 ( 0.7) | 2 ( 0.4) |
| Toxicity Grade 2 | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) |
| Toxicity Grade 3 | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) |
| Toxicity Grade 4 | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) |
| **Creatinine Increased** | | | | |
| Toxicity Grade 1 | 26 (10.2) | 44 (15.8) | 40 (14.4) | 84 (15.1) |
| Toxicity Grade 2 | 6 ( 2.3) | 4 ( 1.4) | 1 ( 0.4) | 5 ( 0.9) |
| Toxicity Grade 3 | 0 ( 0.0) | 0 ( 0.0) | 1 ( 0.4) | 1 ( 0.2) |
| Toxicity Grade 4 | 0 ( 0.0) | 2 ( 0.7) | 0 ( 0.0) | 2 ( 0.4) |
| **Gamma Glutamyl Transferase Increased** | | | | |
| Toxicity Grade 1 | 0 ( 0.0) | 1 ( 0.4) | 1 ( 0.4) | 2 ( 0.4) |
| Toxicity Grade 2 | 1 ( 0.4) | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) |
| Toxicity Grade 3 | 2 ( 0.8) | 1 ( 0.4) | 0 ( 0.0) | 1 ( 0.2) |
| Toxicity Grade 4 | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) |
| **Glucose Decreased** | | | | |
| Toxicity Grade 1 | 5 ( 2.0) | 20 ( 7.2) | 13 ( 4.7) | 33 ( 5.9) |
| Toxicity Grade 2 | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) |
| Toxicity Grade 3 | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) |
| Toxicity Grade 4 | 0 ( 0.0) | 2 ( 0.7) | 0 ( 0.0) | 2 ( 0.4) |



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## 006 試験（APaT 集団）（続き）

| Laboratory Test | Control (N=256) | MK-3475 10 mg/kg Q2W (N=278) | MK-3475 10 mg/kg Q3W (N=277) | MK-3475 combined (N=555) |
|---|---|---|---|---|
| **Glucose Increased** | | | | |
| Toxicity Grade 1 | 82 (32.0) | 118 (42.4 | 121 (43.7 | 239 (43.1 |
| Toxicity Grade 2 | 27 (10.5) | 32 (11.5) | 22 ( 7.9) | 54 ( 9.7) |
| Toxicity Grade 3 | 7 ( 2.7) | 13 ( 4.7) | 9 ( 3.2) | 22 ( 4.0) |
| Toxicity Grade 4 | 0 ( 0.0) | 1 ( 0.4) | 0 ( 0.0) | 1 ( 0.2) |
| **Hemoglobin Decreased** | | | | |
| Toxicity Grade 1 | 82 (32.0) | 99 (35.6) | 103 (37.2 | 202 (36.4 |
| Toxicity Grade 2 | 22 ( 8.6) | 24 ( 8.6) | 22 ( 7.9) | 46 ( 8.3) |
| Toxicity Grade 3 | 2 ( 0.8) | 10 ( 3.6) | 5 ( 1.8) | 15 ( 2.7) |
| Toxicity Grade 4 | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) |
| **Leukocytes Decreased** | | | | |
| Toxicity Grade 1 | 12 ( 4.7) | 35 (12.6) | 29 (10.5) | 64 (11.5) |
| Toxicity Grade 2 | 2 ( 0.8) | 8 ( 2.9) | 3 ( 1.1) | 11 ( 2.0) |
| Toxicity Grade 3 | 0 ( 0.0) | 1 ( 0.4) | 0 ( 0.0) | 1 ( 0.2) |
| Toxicity Grade 4 | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) |
| **Lymphocytes Decreased** | | | | |
| Toxicity Grade 1 | 34 (13.3) | 62 (22.3) | 60 (21.7) | 122 (22.0 |
| Toxicity Grade 2 | 21 ( 8.2) | 43 (15.5) | 38 (13.7) | 81 (14.6) |
| Toxicity Grade 3 | 4 ( 1.6) | 11 ( 4.0) | 8 ( 2.9) | 19 ( 3.4) |
| Toxicity Grade 4 | 0 ( 0.0) | 4 ( 1.4) | 5 ( 1.8) | 9 ( 1.6) |
| **Magnesium Decreased** | | | | |
| Toxicity Grade 1 | 26 (10.2) | 33 (11.9) | 36 (13.0) | 69 (12.4) |
| Toxicity Grade 2 | 4 ( 1.6) | 7 ( 2.5) | 3 ( 1.1) | 10 ( 1.8) |
| Toxicity Grade 3 | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) |
| Toxicity Grade 4 | 0 ( 0.0) | 1 ( 0.4) | 0 ( 0.0) | 1 ( 0.2) |



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## 006 試験（APaT 集団）（続き）

| Laboratory Test | Control (N=256) | MK-3475 10 mg/kg Q2W (N=278) | MK-3475 10 mg/kg Q3W (N=277) | MK-3475 combined (N=555) |
|---|---|---|---|---|
| **Magnesium Increased** | | | | |
| Toxicity Grade 1 | 8 ( 3.1) | 11 ( 4.0) | 22 ( 7.9) | 33 ( 5.9) |
| Toxicity Grade 2 | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) |
| Toxicity Grade 3 | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) |
| Toxicity Grade 4 | 0 ( 0.0) | 4 ( 1.4) | 1 ( 0.4) | 5 ( 0.9) |
| **Neutrophils Decreased** | | | | |
| Toxicity Grade 1 | 10 ( 3.9) | 20 ( 7.2) | 10 ( 3.6) | 30 ( 5.4) |
| Toxicity Grade 2 | 2 ( 0.8) | 8 ( 2.9) | 3 ( 1.1) | 11 ( 2.0) |
| Toxicity Grade 3 | 1 ( 0.4) | 3 ( 1.1) | 2 ( 0.7) | 5 ( 0.9) |
| Toxicity Grade 4 | 0 ( 0.0) | 4 ( 1.4) | 3 ( 1.1) | 7 ( 1.3) |
| **Phosphate Decreased** | | | | |
| Toxicity Grade 1 | 4 ( 1.6) | 9 ( 3.2) | 9 ( 3.2) | 18 ( 3.2) |
| Toxicity Grade 2 | 15 ( 5.9) | 28 (10.1) | 37 (13.4) | 65 (11.7) |
| Toxicity Grade 3 | 4 ( 1.6) | 11 ( 4.0) | 9 ( 3.2) | 20 ( 3.6) |
| Toxicity Grade 4 | 0 ( 0.0) | 0 ( 0.0) | 1 ( 0.4) | 1 ( 0.2) |
| **Platelet Decreased** | | | | |
| Toxicity Grade 1 | 8 ( 3.1) | 33 (11.9) | 30 (10.8) | 63 (11.4) |
| Toxicity Grade 2 | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) |
| Toxicity Grade 3 | 0 ( 0.0) | 0 ( 0.0) | 1 ( 0.4) | 1 ( 0.2) |
| Toxicity Grade 4 | 1 ( 0.4) | 4 ( 1.4) | 1 ( 0.4) | 5 ( 0.9) |
| **Potassium Decreased** | | | | |
| Toxicity Grade 1 | 17 ( 6.6) | 37 (13.3) | 24 ( 8.7) | 61 (11.0) |
| Toxicity Grade 2 | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) |
| Toxicity Grade 3 | 2 ( 0.8) | 4 ( 1.4) | 2 ( 0.7) | 6 ( 1.1) |
| Toxicity Grade 4 | 2 ( 0.8) | 1 ( 0.4) | 1 ( 0.4) | 2 ( 0.4) |



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## 006 試験（APaT 集団）（続き）

| Laboratory Test | Control (N=256) | MK-3475 10 mg/kg Q2W (N=278) | MK-3475 10 mg/kg Q3W (N=277) | MK-3475 combined (N=555) |
|---|---|---|---|---|
| **Potassium Increased** | | | | |
| Toxicity Grade 1 | 9 ( 3.5) | 32 (11.5) | 24 ( 8.7) | 56 (10.1) |
| Toxicity Grade 2 | 2 ( 0.8) | 5 ( 1.8) | 3 ( 1.1) | 8 ( 1.4) |
| Toxicity Grade 3 | 1 ( 0.4) | 0 ( 0.0) | 4 ( 1.4) | 4 ( 0.7) |
| Toxicity Grade 4 | 1 ( 0.4) | 2 ( 0.7) | 3 ( 1.1) | 5 ( 0.9) |
| **Prothrombin Intl. Normalized Ratio Incre** | | | | |
| Toxicity Grade 1 | 0 ( 0.0) | 1 ( 0.4) | 1 ( 0.4) | 2 ( 0.4) |
| Toxicity Grade 2 | 0 ( 0.0) | 1 ( 0.4) | 0 ( 0.0) | 1 ( 0.2) |
| Toxicity Grade 3 | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) |
| Toxicity Grade 4 | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) |
| **Sodium Decreased** | | | | |
| Toxicity Grade 1 | 38 (14.8) | 71 (25.5) | 60 (21.7) | 131 (23.6 |
| Toxicity Grade 2 | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) |
| Toxicity Grade 3 | 4 ( 1.6) | 4 ( 1.4) | 4 ( 1.4) | 8 ( 1.4) |
| Toxicity Grade 4 | 3 ( 1.2) | 3 ( 1.1) | 6 ( 2.2) | 9 ( 1.6) |
| **Sodium Increased** | | | | |
| Toxicity Grade 1 | 7 ( 2.7) | 25 ( 9.0) | 21 ( 7.6) | 46 ( 8.3) |
| Toxicity Grade 2 | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) |
| Toxicity Grade 3 | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) |
| Toxicity Grade 4 | 0 ( 0.0) | 2 ( 0.7) | 0 ( 0.0) | 2 ( 0.4) |
| **Triacylglycerol Lipase Increased** | | | | |
| Toxicity Grade 1 | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) |
| Toxicity Grade 2 | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) |
| Toxicity Grade 3 | 0 ( 0.0) | 0 ( 0.0) | 1 ( 0.4) | 1 ( 0.2) |
| Toxicity Grade 4 | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) |



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## 006 試験（APaT 集団）（続き）

| Laboratory Test | Control (N=256) | MK-3475 10 mg/kg Q2W (N=278) | MK-3475 10 mg/kg Q3W (N=277) | MK-3475 combined (N=555) |
|---|---|---|---|---|
| **Triglycerides** | | | | |
| Toxicity Grade 1 | 90 (35.2) | 125 (45.0 | 113 (40.8 | 238 (42.9 |
| Toxicity Grade 2 | 16 ( 6.3) | 29 (10.4) | 28 (10.1) | 57 (10.3) |
| Toxicity Grade 3 | 2 ( 0.8) | 6 ( 2.2) | 7 ( 2.5) | 13 ( 2.3) |
| Toxicity Grade 4 | 0 ( 0.0) | 1 ( 0.4) | 1 ( 0.4) | 2 ( 0.4) |
| If a patient had more than one graded abnormalities for a lab test, only the hightest grade is counted.<br>Grades are based on NCI CTCAE version 4.<br>(Database Cutoff Date: 03SEP2014) | | | | |

Data Source: [資料5.3.5.1.2: P006V01]



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## 付録 2.7.4-128 臨床検査値異常の最大 Grade の要約

## 006 試験（MK-3475 併合）（APaT 集団）

| | Control (N=256) | | | | | | | | MK-3475 combined (N=555) | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Grade 1 | | Grade 2 | | Grade 3 | | Grade 4 | | Grade 1 | | Grade 2 | | Grade 3 | | Grade 4 | |
| | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) |
| **Chemistry** | | | | | | | | | | | | | | | | |
| Alanine Aminotransferase | 65 | (25.4) | 2 | (0.8) | 10 | (3.9) | 1 | (0.4) | 132 | (23.8) | 12 | (2.2) | 14 | (2.5) | 3 | (0.5) |
| Albumin | 58 | (22.7) | 35 | (13.7) | 3 | (1.2) | 0 | (0.0) | 97 | (17.5) | 65 | (11.7) | 13 | (2.3) | 0 | (0.0) |
| Alkaline Phosphatase | 60 | (23.4) | 15 | (5.9) | 6 | (2.3) | 0 | (0.0) | 122 | (22.0) | 23 | (4.1) | 14 | (2.5) | 0 | (0.0) |
| Amylase | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 2 | (0.4) | 0 | (0.0) |
| Aspartate Aminotransferase | 60 | (23.4) | 8 | (3.1) | 6 | (2.3) | 0 | (0.0) | 150 | (27.0) | 16 | (2.9) | 10 | (1.8) | 4 | (0.7) |
| Bilirubin | 14 | (5.5) | 7 | (2.7) | 2 | (0.8) | 1 | (0.4) | 44 | (7.9) | 18 | (3.2) | 8 | (1.4) | 0 | (0.0) |
| Calcium | 45 | (17.6) | 12 | (4.7) | 5 | (2.0) | 2 | (0.8) | 131 | (23.6) | 17 | (3.1) | 7 | (1.3) | 13 | (2.3) |
| Cholesterol | 88 | (34.4) | 4 | (1.6) | 0 | (0.0) | 0 | (0.0) | 216 | (38.9) | 21 | (3.8) | 1 | (0.2) | 5 | (0.9) |
| Creatine Kinase | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 2 | (0.4) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) |
| Creatinine | 31 | (12.1) | 9 | (3.5) | 2 | (0.8) | 1 | (0.4) | 88 | (15.9) | 11 | (2.0) | 2 | (0.4) | 3 | (0.5) |
| Gamma Glutamyl Transferase | 0 | (0.0) | 0 | (0.0) | 7 | (2.7) | 0 | (0.0) | 3 | (0.5) | 2 | (0.4) | 2 | (0.4) | 1 | (0.2) |
| Glucose | 110 | (43.0) | 40 | (15.6) | 9 | (3.5) | 1 | (0.4) | 273 | (49.2) | 63 | (11.4) | 25 | (4.5) | 4 | (0.7) |
| Hemoglobin | 0 | (0.0) | 1 | (0.4) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.2) | 1 | (0.2) | 0 | (0.0) |
| Magnesium | 54 | (21.1) | 4 | (1.6) | 0 | (0.0) | 0 | (0.0) | 111 | (20.0) | 11 | (2.0) | 0 | (0.0) | 7 | (1.3) |
| Phosphate | 4 | (1.6) | 26 | (10.2) | 11 | (4.3) | 0 | (0.0) | 20 | (3.6) | 73 | (13.2) | 23 | (4.1) | 1 | (0.2) |



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## 付録 2.7.4-128 臨床検査値異常の最大 Grade の要約

## 006 試験（MK-3475 併合）（APaT 集団）（続き）

| | Control (N=256) | | | | | | | | MK-3475 combined (N=555) | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Grade 1 | | Grade 2 | | Grade 3 | | Grade 4 | | Grade 1 | | Grade 2 | | Grade 3 | | Grade 4 | |
| | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) |
| **Chemistry** | | | | | | | | | | | | | | | | |
| Platelet | 1 | (0.4) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) |
| Potassium | 43 | (16.8) | 4 | (1.6) | 6 | (2.3) | 4 | (1.6) | 124 | (22.3) | 11 | (2.0) | 10 | (1.8) | 8 | (1.4) |
| Sodium | 77 | (30.1) | 0 | (0.0) | 16 | (6.3) | 5 | (2.0) | 204 | (36.8) | 0 | (0.0) | 17 | (3.1) | 13 | (2.3) |
| Triacylglycerol Lipase | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.2) | 1 | (0.2) | 1 | (0.2) |
| Triglycerides | 70 | (27.3) | 13 | (5.1) | 2 | (0.8) | 0 | (0.0) | 175 | (31.5) | 38 | (6.8) | 7 | (1.3) | 2 | (0.4) |
| **Hematology** | | | | | | | | | | | | | | | | |
| Activated Partial Thromboplastin Time | 26 | (10.2) | 2 | (0.8) | 1 | (0.4) | 0 | (0.0) | 50 | (9.0) | 3 | (0.5) | 23 | (4.1) | 0 | (0.0) |
| Alanine Aminotransferase | 0 | (0.0) | 1 | (0.4) | 1 | (0.4) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) |
| Albumin | 0 | (0.0) | 2 | (0.8) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) |
| Aspartate Aminotransferase | 0 | (0.0) | 1 | (0.4) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) |
| Calcium | 2 | (0.8) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) |
| Fibrinogen | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (0.4) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) |
| Gamma Glutamyl Transferase | 0 | (0.0) | 1 | (0.4) | 1 | (0.4) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) |



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## 付録 2.7.4-128 臨床検査値異常の最大 Grade の要約

## 006 試験（MK-3475 併合）（APaT 集団）（続き）

| | Control (N=256) | | | | | | | | MK-3475 combined (N=555) | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Grade 1 | | Grade 2 | | Grade 3 | | Grade 4 | | Grade 1 | | Grade 2 | | Grade 3 | | Grade 4 | |
| | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) |
| **Hematology** | | | | | | | | | | | | | | | | |
| Hemoglobin | 96 | (37.5) | 27 | (10.5) | 11 | (4.3) | 0 | (0.0) | 216 | (38.9) | 53 | (9.5) | 20 | (3.6) | 0 | (0.0) |
| Leukocytes | 18 | (7.0) | 3 | (1.2) | 0 | (0.0) | 0 | (0.0) | 68 | (12.3) | 13 | (2.3) | 2 | (0.4) | 0 | (0.0) |
| Lymphocytes | 43 | (16.8) | 33 | (12.9) | 14 | (5.5) | 0 | (0.0) | 125 | (22.5) | 100 | (18.0) | 25 | (4.5) | 1 | (0.2) |
| Lymphocytes/Leukocytes | 3 | (1.2) | 11 | (4.3) | 5 | (2.0) | 2 | (0.8) | 6 | (1.1) | 33 | (5.9) | 15 | (2.7) | 8 | (1.4) |
| Neutrophils | 11 | (4.3) | 1 | (0.4) | 0 | (0.0) | 0 | (0.0) | 29 | (5.2) | 13 | (2.3) | 6 | (1.1) | 2 | (0.4) |
| Neutrophils/Leukocytes | 6 | (2.3) | 1 | (0.4) | 3 | (1.2) | 0 | (0.0) | 7 | (1.3) | 3 | (0.5) | 3 | (0.5) | 7 | (1.3) |
| Platelet | 17 | (6.6) | 1 | (0.4) | 1 | (0.4) | 1 | (0.4) | 73 | (13.2) | 1 | (0.2) | 0 | (0.0) | 6 | (1.1) |
| Prothrombin Intl. Normalized Ratio | 1 | (0.4) | 1 | (0.4) | 0 | (0.0) | 0 | (0.0) | 6 | (1.1) | 2 | (0.4) | 2 | (0.4) | 0 | (0.0) |
| **Serology** | | | | | | | | | | | | | | | | |
| Alanine Aminotransferase | 1 | (0.4) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) |
| **Other** | | | | | | | | | | | | | | | | |



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## 付録 2.7.4-128 臨床検査値異常の最大 Grade の要約

## 006 試験（MK-3475 併合）（APaT 集団）（続き）

| | Control (N=256) | | | | | | | | MK-3475 combined (N=555) | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Grade 1 | | Grade 2 | | Grade 3 | | Grade 4 | | Grade 1 | | Grade 2 | | Grade 3 | | Grade 4 | |
| | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) |
| **Other** | | | | | | | | | | | | | | | | |
| Triglycerides | 28 | (10.9) | 8 | (3.1) | 0 | (0.0) | 0 | (0.0) | 74 | (13.3) | 22 | (4.0) | 5 | (0.9) | 0 | (0.0) |

If a patient had more than one graded abnormalities for a lab test, only the highest grade is counted.
Grades are based on NCI CTCAE version 4.0.
(Database Cutoff Date: 03SEP2014).

Data Source: [資料5.3.5.1.2: P006V01]



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## 付録 2.7.4-129 臨床検査値の Grade がベースラインより悪化した患者の要約

## 041 試験（APaT 集団）

| Laboratory Test | Subjects With Advanced Melanoma (N=42) |
|---|---|
| **Alanine Aminotransferase Increased** | |
| Improved from baseline | 0 (0.0) |
| Worsened from baseline | 9 (21.4) |
| Clinically meaningful† worsened from baseline | 1 (2.4) |
| **Albumin Decreased** | |
| Improved from baseline | 1 (2.4) |
| Worsened from baseline | 23 (54.8) |
| Clinically meaningful† worsened from baseline | 4 (9.5) |
| **Alkaline Phosphatase Increased** | |
| Improved from baseline | 0 (0.0) |
| Worsened from baseline | 11 (26.2) |
| Clinically meaningful† worsened from baseline | 1 (2.4) |
| **Aspartate Aminotransferase Increased** | |
| Improved from baseline | 0 (0.0) |
| Worsened from baseline | 14 (33.3) |
| Clinically meaningful† worsened from baseline | 1 (2.4) |
| **Bilirubinn Increased** | |
| Improved from baseline | 0 (0.0) |
| Worsened from baseline | 5 (11.9) |
| Clinically meaningful† worsened from baseline | 1 (2.4) |



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## 付録 2.7.4-129 臨床検査値の Grade がベースラインより悪化した患者の要約

## 041 試験（APaT 集団）（続き）

| Laboratory Test | Subjects With Advanced Melanoma (N=42) |
|---|---|
| **Calcium Decreased** | |
| Improved from baseline | 0 (0.0) |
| Worsened from baseline | 9 (21.4) |
| Clinically meaningful† worsened from baseline | 1 (2.4) |
| **Gamma Glutamyl Transferase Increased** | |
| Improved from baseline | 0 (0.0) |
| Worsened from baseline | 2 (4.8) |
| Clinically meaningful† worsened from baseline | 1 (2.4) |
| **Glucose Increased** | |
| Improved from baseline | 0 (0.0) |
| Worsened from baseline | 34 (81.0) |
| Clinically meaningful† worsened from baseline | 7 (16.7) |
| **Hemoglobin Decreased** | |
| Improved from baseline | 0 (0.0) |
| Worsened from baseline | 17 (40.5) |
| Clinically meaningful† worsened from baseline | 5 (11.9) |
| **Leukocytes Decreased** | |
| Improved from baseline | 0 (0.0) |
| Worsened from baseline | 5 (11.9) |
| Clinically meaningful† worsened from baseline | 2 (4.8) |



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## 付録 2.7.4-129 臨床検査値の Grade がベースラインより悪化した患者の要約

### 041 試験（APaT 集団）（続き）

| Laboratory Test | Subjects With Advanced Melanoma (N=42) |
|---|---|
| **Lymphocytes Decreased** | |
| Improved from baseline | 0 (0.0) |
| Worsened from baseline | 1 (2.4) |
| Clinically meaningful† worsened from baseline | 1 (2.4) |
| **Magnesium Decreased** | |
| Improved from baseline | 0 (0.0) |
| Worsened from baseline | 6 (14.3) |
| Clinically meaningful† worsened from baseline | 1 (2.4) |
| **Phosphate Decreased** | |
| Improved from baseline | 0 (0.0) |
| Worsened from baseline | 13 (31.0) |
| Clinically meaningful† worsened from baseline | 9 (21.4) |
| **Potassium Increased** | |
| Improved from baseline | 0 (0.0) |
| Worsened from baseline | 12 (28.6) |
| Clinically meaningful† worsened from baseline | 1 (2.4) |
| **Sodium Decreased** | |
| Improved from baseline | 0 (0.0) |
| Worsened from baseline | 12 (28.6) |



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## 付録 2.7.4-129 臨床検査値の Grade がベースラインより悪化した患者の要約

### 041 試験（APaT 集団）（続き）

| Laboratory Test | Subjects With Advanced Melanoma (N=42) |
|---|---|
| **Sodium Decreased** | |
| Clinically meaningful† worsened from baseline | 5 (11.9) |

A missing baseline value was set to Grade 0.

† A clinically meaningful worsening in CTCAE grade was defined as a shift from less than Grade 3 to Grade 3, 4 or 5 or a shift from Grade 0 to Grade 2.

(Database Cutoff Date: [redacted]

Data Source: [資料5.3.5.2.3: P041V01]



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## 付録 2.7.4-130 臨床検査値の Grade がベースラインより悪化した患者での臨床検査値異常の最大 Grade の要約
## 041 試験（APaT 集団）

| Laboratory Test | Subjects With Advanced Melanoma (N=42) |
|---|---|
| **Activated Partial Thromboplastin Time In** | |
| Toxicity Grade 1 | 2 ( 4.8) |
| Toxicity Grade 2 | 0 ( 0.0) |
| Toxicity Grade 3 | 0 ( 0.0) |
| Toxicity Grade 4 | 0 ( 0.0) |
| **Alanine Aminotransferase Increased** | |
| Toxicity Grade 1 | 7 (16.7) |
| Toxicity Grade 2 | 1 ( 2.4) |
| Toxicity Grade 3 | 1 ( 2.4) |
| Toxicity Grade 4 | 0 ( 0.0) |
| **Albumin Decreased** | |
| Toxicity Grade 1 | 17 (40.5) |
| Toxicity Grade 2 | 5 (11.9) |
| Toxicity Grade 3 | 1 ( 2.4) |
| Toxicity Grade 4 | 0 ( 0.0) |
| **Alkaline Phosphatase Increased** | |
| Toxicity Grade 1 | 9 (21.4) |
| Toxicity Grade 2 | 1 ( 2.4) |
| Toxicity Grade 3 | 1 ( 2.4) |
| Toxicity Grade 4 | 0 ( 0.0) |
| **Aspartate Aminotransferase Increased** | |
| Toxicity Grade 1 | 12 (28.6) |
| Toxicity Grade 2 | 1 ( 2.4) |


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## 付録 2.7.4-130 臨床検査値の Grade がベースラインより悪化した患者での臨床検査値異常の最大 Grade の要約
## 041 試験（APaT 集団）（続き）

| Laboratory Test | Subjects With Advanced Melanoma (N=42) |
|---|---|
| Toxicity Grade 3 | 1 ( 2.4) |
| Toxicity Grade 4 | 0 ( 0.0) |
| **Bilirubinn Increased** | |
| Toxicity Grade 1 | 3 ( 7.1) |
| Toxicity Grade 2 | 1 ( 2.4) |
| Toxicity Grade 3 | 0 ( 0.0) |
| Toxicity Grade 4 | 1 ( 2.4) |
| **Calcium Decreased** | |
| Toxicity Grade 1 | 8 (19.0) |
| Toxicity Grade 2 | 0 ( 0.0) |
| Toxicity Grade 3 | 0 ( 0.0) |
| Toxicity Grade 4 | 1 ( 2.4) |
| **Creatinine Increased** | |
| Toxicity Grade 1 | 5 (11.9) |
| Toxicity Grade 2 | 0 ( 0.0) |
| Toxicity Grade 3 | 0 ( 0.0) |
| Toxicity Grade 4 | 0 ( 0.0) |
| **Gamma Glutamyl Transferase Increased** | |
| Toxicity Grade 1 | 1 ( 2.4) |
| Toxicity Grade 2 | 0 ( 0.0) |
| Toxicity Grade 3 | 0 ( 0.0) |
| Toxicity Grade 4 | 1 ( 2.4) |
| **Glucose Decreased** | |



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## 付録 2.7.4-130 臨床検査値の Grade がベースラインより悪化した患者での臨床検査値異常の最大 Grade の要約
## 041 試験（APaT 集団）（続き）

| Laboratory Test | Subjects With Advanced Melanoma (N=42) |
|---|---|
| Toxicity Grade 1 | 5 (11.9) |
| Toxicity Grade 2 | 0 ( 0.0) |
| Toxicity Grade 3 | 0 ( 0.0) |
| Toxicity Grade 4 | 0 ( 0.0) |
| **Glucose Increased** | |
| Toxicity Grade 1 | 22 (52.4) |
| Toxicity Grade 2 | 9 (21.4) |
| Toxicity Grade 3 | 1 ( 2.4) |
| Toxicity Grade 4 | 2 ( 4.8) |
| **Hemoglobin Decreased** | |
| Toxicity Grade 1 | 10 (23.8) |
| Toxicity Grade 2 | 3 ( 7.1) |
| Toxicity Grade 3 | 4 ( 9.5) |
| Toxicity Grade 4 | 0 ( 0.0) |
| **Leukocytes Decreased** | |
| Toxicity Grade 1 | 3 ( 7.1) |
| Toxicity Grade 2 | 2 ( 4.8) |
| Toxicity Grade 3 | 0 ( 0.0) |
| Toxicity Grade 4 | 0 ( 0.0) |
| **Lymphocytes Decreased** | |
| Toxicity Grade 1 | 0 ( 0.0) |
| Toxicity Grade 2 | 0 ( 0.0) |
| Toxicity Grade 3 | 1 ( 2.4) |


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## 付録 2.7.4-130 臨床検査値の Grade がベースラインより悪化した患者での臨床検査値異常の最大 Grade の要約
## 041 試験（APaT 集団）（続き）

| Laboratory Test | Subjects With Advanced Melanoma (N=42) |
|---|---|
| Toxicity Grade 4 | 0 ( 0.0) |
| **Magnesium Decreased** | |
| Toxicity Grade 1 | 5 (11.9) |
| Toxicity Grade 2 | 1 ( 2.4) |
| Toxicity Grade 3 | 0 ( 0.0) |
| Toxicity Grade 4 | 0 ( 0.0) |
| **Magnesium Increased** | |
| Toxicity Grade 1 | 3 ( 7.1) |
| Toxicity Grade 2 | 0 ( 0.0) |
| Toxicity Grade 3 | 0 ( 0.0) |
| Toxicity Grade 4 | 0 ( 0.0) |
| **Neutrophils Decreased** | |
| Toxicity Grade 1 | 2 ( 4.8) |
| Toxicity Grade 2 | 0 ( 0.0) |
| Toxicity Grade 3 | 0 ( 0.0) |
| Toxicity Grade 4 | 0 ( 0.0) |
| **Phosphate Decreased** | |
| Toxicity Grade 1 | 3 ( 7.1) |
| Toxicity Grade 2 | 10 (23.8) |
| Toxicity Grade 3 | 0 ( 0.0) |
| Toxicity Grade 4 | 0 ( 0.0) |
| **Platelet Decreased** | |
| Toxicity Grade 1 | 8 (19.0) |


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## 付録 2.7.4-130 臨床検査値の Grade がベースラインより悪化した患者での臨床検査値異常の最大 Grade の要約
## 041 試験（APaT 集団）（続き）

| Laboratory Test | Subjects With Advanced Melanoma (N=42) |
|---|---|
| Toxicity Grade 2 | 0 ( 0.0) |
| Toxicity Grade 3 | 0 ( 0.0) |
| Toxicity Grade 4 | 0 ( 0.0) |
| **Potassium Decreased** | |
| Toxicity Grade 1 | 4 ( 9.5) |
| Toxicity Grade 2 | 0 ( 0.0) |
| Toxicity Grade 3 | 0 ( 0.0) |
| Toxicity Grade 4 | 0 ( 0.0) |
| **Potassium Increased** | |
| Toxicity Grade 1 | 11 (26.2) |
| Toxicity Grade 2 | 0 ( 0.0) |
| Toxicity Grade 3 | 1 ( 2.4) |
| Toxicity Grade 4 | 0 ( 0.0) |
| **Prothrombin Intl. Normalized Ratio Incre** | |
| Toxicity Grade 1 | 3 ( 7.1) |
| Toxicity Grade 2 | 1 ( 2.4) |
| Toxicity Grade 3 | 0 ( 0.0) |
| Toxicity Grade 4 | 0 ( 0.0) |
| **Sodium Decreased** | |
| Toxicity Grade 1 | 7 (16.7) |
| Toxicity Grade 2 | 0 ( 0.0) |
| Toxicity Grade 3 | 4 ( 9.5) |
| Toxicity Grade 4 | 1 ( 2.4) |


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## 付録 2.7.4-130 臨床検査値の Grade がベースラインより悪化した患者での臨床検査値異常の最大 Grade の要約
## 041 試験（APaT 集団）（続き）

| Laboratory Test | Subjects With Advanced Melanoma (N=42) |
|---|---|
| **Sodium Increased** | |
| Toxicity Grade 1 | 2 ( 4.8) |
| Toxicity Grade 2 | 0 ( 0.0) |
| Toxicity Grade 3 | 0 ( 0.0) |
| Toxicity Grade 4 | 0 ( 0.0) |
| If a patient had more than one graded abnormalities for a lab test, only the hightest grade is counted.<br>Grades are based on NCI CTCAE version 4.0.<br>(Database Cutoff Date: [redacted]. | |

Data Source: [資料5.3.5.2.3: P041V01]



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## 付録 2.7.4-131 有害事象の要約（年齢別）

### 001 試験パート B2+D（APaT 集団）

| | Ipi-naïve 2 mg/kg Q3W | | | | Ipi-naïve 10 mg/kg Q3W | | | | Ipi-exposed 2 mg/kg Q3W | | | | Ipi-exposed 10 mg/kg Q3W | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | < 65 | | >=65 | | < 65 | | >=65 | | < 65 | | >=65 | | < 65 | | >=65 | |
| | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) |
| Patients in population | 33 | | 18 | | 33 | | 19 | | 60 | | 29 | | 51 | | 33 | |
| with one or more adverse events | 33 | (100.0) | 18 | (100.0) | 33 | (100.0) | 18 | (94.7) | 60 | (100.0) | 28 | (96.6) | 50 | (98.0) | 32 | (97.0) |
| with no adverse event | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 1 | (5.3) | 0 | (0.0) | 1 | (3.4) | 1 | (2.0) | 1 | (3.0) |
| with drug-related† adverse events | 28 | (84.8) | 16 | (88.9) | 30 | (90.9) | 17 | (89.5) | 50 | (83.3) | 25 | (86.2) | 39 | (76.5) | 31 | (93.9) |
| with Grade 3- 5 adverse events | 13 | (39.4) | 6 | (33.3) | 17 | (51.5) | 5 | (26.3) | 24 | (40.0) | 13 | (44.8) | 24 | (47.1) | 16 | (48.5) |
| with Grade 3- 5 drug-related adverse events | 8 | (24.2) | 4 | (22.2) | 1 | (3.0) | 1 | (5.3) | 9 | (15.0) | 6 | (20.7) | 3 | (5.9) | 7 | (21.2) |
| with serious adverse events | 11 | (33.3) | 3 | (16.7) | 13 | (39.4) | 5 | (26.3) | 16 | (26.7) | 11 | (37.9) | 20 | (39.2) | 13 | (39.4) |
| with serious drug-related adverse events | 5 | (15.2) | 2 | (11.1) | 2 | (6.1) | 1 | (5.3) | 2 | (3.3) | 5 | (17.2) | 1 | (2.0) | 4 | (12.1) |
| who died | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) |
| with drug-related death | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) |
| discontinued‡ due to an adverse event | 1 | (3.0) | 1 | (5.6) | 3 | (9.1) | 2 | (10.5) | 2 | (3.3) | 3 | (10.3) | 5 | (9.8) | 5 | (15.2) |
| discontinued due to a drug-related adverse event | 0 | (0.0) | 1 | (5.6) | 1 | (3.0) | 2 | (10.5) | 1 | (1.7) | 2 | (6.9) | 1 | (2.0) | 2 | (6.1) |
| discontinued due to a serious adverse event | 1 | (3.0) | 1 | (5.6) | 1 | (3.0) | 1 | (5.3) | 1 | (1.7) | 2 | (6.9) | 2 | (3.9) | 2 | (6.1) |



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## 付録 2.7.4-131 有害事象の要約（年齢別）

### 001 試験パート B2+D（APaT 集団）（続き）

| | Total | | | |
|---|---|---|---|---|
| | < 65 | | >=65 | |
| | n | (%) | n | (%) |
| Patients in population | 177 | | 99 | |
| with one or more adverse events | 176 | (99.4) | 96 | (97.0) |
| with no adverse event | 1 | (0.6) | 3 | (3.0) |
| with drug-related[†] adverse events | 147 | (83.1) | 89 | (89.9) |
| with Grade 3- 5 adverse events | 78 | (44.1) | 40 | (40.4) |
| with Grade 3- 5 drug-related adverse events | 21 | (11.9) | 18 | (18.2) |
| with serious adverse events | 60 | (33.9) | 32 | (32.3) |
| with serious drug-related adverse events | 10 | (5.6) | 12 | (12.1) |
| who died | 0 | (0.0) | 0 | (0.0) |
| with drug-related death | 0 | (0.0) | 0 | (0.0) |
| discontinued[‡] due to an adverse event | 11 | (6.2) | 11 | (11.1) |
| discontinued due to a drug-related adverse event | 3 | (1.7) | 7 | (7.1) |
| discontinued due to a serious adverse event | 5 | (2.8) | 6 | (6.1) |



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## 付録 2.7.4-131 有害事象の要約（年齢別）
## 001 試験パート B2+D（APaT 集団）（続き）

| | Ipi-naïve 2 mg/kg Q3W | | | | Ipi-naïve 10 mg/kg Q3W | | | | Ipi-exposed 2 mg/kg Q3W | | | | Ipi-exposed 10 mg/kg Q3W | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | < 65 | | >=65 | | < 65 | | >=65 | | < 65 | | >=65 | | < 65 | | >=65 | |
| | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) |
| discontinued due to a serious drug-related adverse event | 0 | (0.0) | 1 | (5.6) | 0 | (0.0) | 1 | (5.3) | 1 | (1.7) | 2 | (6.9) | 0 | (0.0) | 1 | (3.0) |

## 付録 2.7.4-131 有害事象の要約（年齢別）
## 001 試験パート B2+D（APaT 集団）（続き）

| | Total | | | |
|---|---|---|---|---|
| | < 65 | | >=65 | |
| | n | (%) | n | (%) |
| discontinued due to a serious drug-related adverse event | 1 | (0.6) | 5 | (5.1) |

Grades are based on NCI CTCAE version 4.0.
MedDRA preferred terms ‘Progressive Disease’ and ‘Malignant Neoplasm Progression' not related to the drug are excluded.
† Determined by the investigator to be related to the drug.
‡ Study medication withdrawn.
(Database Cutoff Date: [redacted])

Data Source: [資料5.3.5.2.1.2: P001V02]



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## 付録 2.7.4-132 有害事象の要約（年齢別）

### 001 試験パート B3（APaT 集団）

| | MK-3475 10 mg/kg Q3W | | | | MK-3475 10 mg/kg Q2W | | | | Total | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | < 65 | | >=65 | | < 65 | | >=65 | | < 65 | | >=65 | |
| | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) |
| Patients in population | 71 | | 50 | | 76 | | 47 | | 147 | | 97 | |
| with one or more adverse events | 68 | (95.8) | 49 | (98.0) | 76 | (100.0) | 47 | (100.0) | 144 | (98.0) | 96 | (99.0) |
| with no adverse event | 3 | (4.2) | 1 | (2.0) | 0 | (0.0) | 0 | (0.0) | 3 | (2.0) | 1 | (1.0) |
| with drug-related[†] adverse events | 58 | (81.7) | 41 | (82.0) | 65 | (85.5) | 34 | (72.3) | 123 | (83.7) | 75 | (77.3) |
| with Grade 3- 5 adverse events | 24 | (33.8) | 19 | (38.0) | 27 | (35.5) | 26 | (55.3) | 51 | (34.7) | 45 | (46.4) |
| with Grade 3- 5 drug-related adverse events | 8 | (11.3) | 6 | (12.0) | 9 | (11.8) | 10 | (21.3) | 17 | (11.6) | 16 | (16.5) |
| with serious adverse events | 16 | (22.5) | 12 | (24.0) | 20 | (26.3) | 18 | (38.3) | 36 | (24.5) | 30 | (30.9) |
| with serious drug-related adverse events | 6 | (8.5) | 2 | (4.0) | 9 | (11.8) | 3 | (6.4) | 15 | (10.2) | 5 | (5.2) |
| who died | 0 | (0.0) | 2 | (4.0) | 0 | (0.0) | 1 | (2.1) | 0 | (0.0) | 3 | (3.1) |
| with drug-related death | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) |
| discontinued[‡] due to an adverse event | 7 | (9.9) | 4 | (8.0) | 8 | (10.5) | 9 | (19.1) | 15 | (10.2) | 13 | (13.4) |
| discontinued due to a drug-related adverse event | 1 | (1.4) | 0 | (0.0) | 3 | (3.9) | 1 | (2.1) | 4 | (2.7) | 1 | (1.0) |
| discontinued due to a serious adverse event | 5 | (7.0) | 2 | (4.0) | 6 | (7.9) | 6 | (12.8) | 11 | (7.5) | 8 | (8.2) |
| discontinued due to a serious drug-related adverse event | 1 | (1.4) | 0 | (0.0) | 3 | (3.9) | 0 | (0.0) | 4 | (2.7) | 0 | (0.0) |

Grades are based on NCI CTCAE version 4.0.
MedDRA preferred terms ‘Progressive Disease’ and ‘Malignant Neoplasm Progression' not related to the drug are excluded.
[†] Determined by the investigator to be related to the drug.
[‡] Study medication withdrawn.
(Database Cutoff Date: [redacted])

Data Source: [資料5.3.5.2.1.2: P001V02]



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## 付録 2.7.4-133 有害事象の要約（ECOG SP 別）

## 001 試験パート B2+D（APaT 集団）

| | Ipi-naïve 2 mg/kg Q3W | | | | Ipi-naïve 10 mg/kg Q3W | | | | Ipi-exposed 2 mg/kg Q3W | | | | Ipi-exposed 10 mg/kg Q3W | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | [0] Normal Activity | | [1] Symptoms, But Ambulatory | | [0] Normal Activity | | [1] Symptoms, But Ambulatory | | [0] Normal Activity | | [1] Symptoms, But Ambulatory | | [0] Normal Activity | | [1] Symptoms, But Ambulatory | |
| | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) |
| Patients in population | 41 | | 10 | | 46 | | 6 | | 59 | | 30 | | 56 | | 28 | |
| with one or more adverse events | 41 | (100.0) | 10 | (100.0) | 45 | (97.8) | 6 | (100.0) | 58 | (98.3) | 30 | (100.0) | 55 | (98.2) | 27 | (96.4) |
| with no adverse event | 0 | (0.0) | 0 | (0.0) | 1 | (2.2) | 0 | (0.0) | 1 | (1.7) | 0 | (0.0) | 1 | (1.8) | 1 | (3.6) |
| with drug-related† adverse events | 36 | (87.8) | 8 | (80.0) | 42 | (91.3) | 5 | (83.3) | 51 | (86.4) | 24 | (80.0) | 47 | (83.9) | 23 | (82.1) |
| with Grade 3- 5 adverse events | 13 | (31.7) | 6 | (60.0) | 18 | (39.1) | 4 | (66.7) | 20 | (33.9) | 17 | (56.7) | 24 | (42.9) | 16 | (57.1) |
| with Grade 3- 5 drug-related adverse events | 8 | (19.5) | 4 | (40.0) | 2 | (4.3) | 0 | (0.0) | 6 | (10.2) | 9 | (30.0) | 5 | (8.9) | 5 | (17.9) |
| with serious adverse events | 10 | (24.4) | 4 | (40.0) | 15 | (32.6) | 3 | (50.0) | 14 | (23.7) | 13 | (43.3) | 18 | (32.1) | 15 | (53.6) |
| with serious drug-related adverse events | 4 | (9.8) | 3 | (30.0) | 2 | (4.3) | 1 | (16.7) | 4 | (6.8) | 3 | (10.0) | 2 | (3.6) | 3 | (10.7) |
| who died | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) |
| with drug-related death | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) |
| discontinued‡ due to an adverse event | 2 | (4.9) | 0 | (0.0) | 5 | (10.9) | 0 | (0.0) | 3 | (5.1) | 2 | (6.7) | 6 | (10.7) | 4 | (14.3) |
| discontinued due to a drug-related adverse event | 1 | (2.4) | 0 | (0.0) | 3 | (6.5) | 0 | (0.0) | 2 | (3.4) | 1 | (3.3) | 3 | (5.4) | 0 | (0.0) |
| discontinued due to a serious adverse event | 2 | (4.9) | 0 | (0.0) | 2 | (4.3) | 0 | (0.0) | 2 | (3.4) | 1 | (3.3) | 2 | (3.6) | 2 | (7.1) |



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## 付録 2.7.4-133 有害事象の要約（ECOG SP 別）

### 001 試験パート B2+D（APaT 集団）（続き）

| | Total | | | |
|---|---|---|---|---|
| | [0] Normal Activity | | [1] Symptoms, But Ambulatory | |
| | n | (%) | n | (%) |
| Patients in population | 202 | | 74 | |
| with one or more adverse events | 199 | (98.5) | 73 | (98.6) |
| with no adverse event | 3 | (1.5) | 1 | (1.4) |
| with drug-related[†] adverse events | 176 | (87.1) | 60 | (81.1) |
| with Grade 3- 5 adverse events | 75 | (37.1) | 43 | (58.1) |
| with Grade 3- 5 drug-related adverse events | 21 | (10.4) | 18 | (24.3) |
| with serious adverse events | 57 | (28.2) | 35 | (47.3) |
| with serious drug-related adverse events | 12 | (5.9) | 10 | (13.5) |
| who died | 0 | (0.0) | 0 | (0.0) |
| with drug-related death | 0 | (0.0) | 0 | (0.0) |
| discontinued[‡] due to an adverse event | 16 | (7.9) | 6 | (8.1) |
| discontinued due to a drug-related adverse event | 9 | (4.5) | 1 | (1.4) |
| discontinued due to a serious adverse event | 8 | (4.0) | 3 | (4.1) |



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## 付録 2.7.4-133 有害事象の要約（ECOG SP 別）

## 001 試験パート B2+D（APaT 集団）（続き）

| | Ipi-naïve 2 mg/kg Q3W | | | | Ipi-naïve 10 mg/kg Q3W | | | | Ipi-exposed 2 mg/kg Q3W | | | | Ipi-exposed 10 mg/kg Q3W | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | [0] Normal Activity | | [1] Symptoms, But Ambulatory | | [0] Normal Activity | | [1] Symptoms, But Ambulatory | | [0] Normal Activity | | [1] Symptoms, But Ambulatory | | [0] Normal Activity | | [1] Symptoms, But Ambulatory | |
| | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) |
| discontinued due to a serious drug-related adverse event | 1 | (2.4) | 0 | (0.0) | 1 | (2.2) | 0 | (0.0) | 2 | (3.4) | 1 | (3.3) | 1 | (1.8) | 0 | (0.0) |

## 付録 2.7.4-133 有害事象の要約（ECOG SP 別）

## 001 試験パート B2+D（APaT 集団）（続き）

| | Total | | | |
|---|---|---|---|---|
| | [0] Normal Activity | | [1] Symptoms, But Ambulatory | |
| | n | (%) | n | (%) |
| discontinued due to a serious drug-related adverse event | 5 | (2.5) | 1 | (1.4) |

Grades are based on NCI CTCAE version 4.0.
MedDRA preferred terms ‘Progressive Disease’ and ‘Malignant Neoplasm Progression' not related to the drug are excluded.
† Determined by the investigator to be related to the drug.
‡ Study medication withdrawn.
(Database Cutoff Date: [redacted]

Data Source: [資料5.3.5.2.1.2: P001V02]



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## 付録 2.7.4-134 有害事象の要約（ECOG SP 別）

## 001 試験パート B3（APaT 集団）

| | MK-3475 10 mg/kg Q3W | | | | MK-3475 10 mg/kg Q2W | | | | Total | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | [0] Normal Activity | | [1] Symptoms, But Ambulatory | | [0] Normal Activity | | [1] Symptoms, But Ambulatory | | [0] Normal Activity | | [1] Symptoms, But Ambulatory | |
| | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) |
| Patients in population | 73 | | 47 | | 71 | | 52 | | 144 | | 99 | |
| with one or more adverse events | 71 | (97.3) | 46 | (97.9) | 71 | (100.0) | 52 | (100.0) | 142 | (98.6) | 98 | (99.0) |
| with no adverse event | 2 | (2.7) | 1 | (2.1) | 0 | (0.0) | 0 | (0.0) | 2 | (1.4) | 1 | (1.0) |
| with drug-related[†] adverse events | 63 | (86.3) | 36 | (76.6) | 61 | (85.9) | 38 | (73.1) | 124 | (86.1) | 74 | (74.7) |
| with Grade 3- 5 adverse events | 22 | (30.1) | 21 | (44.7) | 25 | (35.2) | 28 | (53.8) | 47 | (32.6) | 49 | (49.5) |
| with Grade 3- 5 drug-related adverse events | 9 | (12.3) | 5 | (10.6) | 11 | (15.5) | 8 | (15.4) | 20 | (13.9) | 13 | (13.1) |
| with serious adverse events | 15 | (20.5) | 13 | (27.7) | 18 | (25.4) | 20 | (38.5) | 33 | (22.9) | 33 | (33.3) |
| with serious drug-related adverse events | 5 | (6.8) | 3 | (6.4) | 7 | (9.9) | 5 | (9.6) | 12 | (8.3) | 8 | (8.1) |
| who died | 1 | (1.4) | 1 | (2.1) | 0 | (0.0) | 1 | (1.9) | 1 | (0.7) | 2 | (2.0) |
| with drug-related death | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) |
| discontinued[‡] due to an adverse event | 4 | (5.5) | 7 | (14.9) | 4 | (5.6) | 13 | (25.0) | 8 | (5.6) | 20 | (20.2) |
| discontinued due to a drug-related adverse event | 1 | (1.4) | 0 | (0.0) | 1 | (1.4) | 3 | (5.8) | 2 | (1.4) | 3 | (3.0) |
| discontinued due to a serious adverse event | 3 | (4.1) | 4 | (8.5) | 2 | (2.8) | 10 | (19.2) | 5 | (3.5) | 14 | (14.1) |
| discontinued due to a serious drug-related adverse event | 1 | (1.4) | 0 | (0.0) | 0 | (0.0) | 3 | (5.8) | 1 | (0.7) | 3 | (3.0) |

Grades are based on NCI CTCAE version 4.0.
MedDRA preferred terms ‘Progressive Disease’ and ‘Malignant Neoplasm Progression' not related to the drug are excluded.
[†] Determined by the investigator to be related to the drug.
[‡] Study medication withdrawn.
(Database Cutoff Date: [redacted]

Data Source: [資料5.3.5.2.1.2: P001V02]



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## 付録 2.7.4-135 有害事象の要約（男女別）

## 001 試験パート B2+D（APaT 集団）

| | Ipi-naïve 2 mg/kg Q3W | | | | Ipi-naïve 10 mg/kg Q3W | | | | Ipi-exposed 2 mg/kg Q3W | | | | Ipi-exposed 10 mg/kg Q3W | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Male | | Female | | Male | | Female | | Male | | Female | | Male | | Female | |
| | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) |
| Patients in population | 32 | | 19 | | 31 | | 21 | | 47 | | 42 | | 57 | | 27 | |
| with one or more adverse events | 32 | (100.0) | 19 | (100.0) | 30 | (96.8) | 21 | (100.0) | 46 | (97.9) | 42 | (100.0) | 56 | (98.2) | 26 | (96.3) |
| with no adverse event | 0 | (0.0) | 0 | (0.0) | 1 | (3.2) | 0 | (0.0) | 1 | (2.1) | 0 | (0.0) | 1 | (1.8) | 1 | (3.7) |
| with drug-related[†] adverse events | 27 | (84.4) | 17 | (89.5) | 29 | (93.5) | 18 | (85.7) | 40 | (85.1) | 35 | (83.3) | 48 | (84.2) | 22 | (81.5) |
| with Grade 3- 5 adverse events | 12 | (37.5) | 7 | (36.8) | 10 | (32.3) | 12 | (57.1) | 21 | (44.7) | 16 | (38.1) | 30 | (52.6) | 10 | (37.0) |
| with Grade 3- 5 drug-related adverse events | 8 | (25.0) | 4 | (21.1) | 1 | (3.2) | 1 | (4.8) | 8 | (17.0) | 7 | (16.7) | 9 | (15.8) | 1 | (3.7) |
| with serious adverse events | 7 | (21.9) | 7 | (36.8) | 7 | (22.6) | 11 | (52.4) | 17 | (36.2) | 10 | (23.8) | 25 | (43.9) | 8 | (29.6) |
| with serious drug-related adverse events | 5 | (15.6) | 2 | (10.5) | 2 | (6.5) | 1 | (4.8) | 3 | (6.4) | 4 | (9.5) | 4 | (7.0) | 1 | (3.7) |
| who died | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) |
| with drug-related death | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) |
| discontinued[‡] due to an adverse event | 2 | (6.3) | 0 | (0.0) | 2 | (6.5) | 3 | (14.3) | 2 | (4.3) | 3 | (7.1) | 6 | (10.5) | 4 | (14.8) |
| discontinued due to a drug-related adverse event | 1 | (3.1) | 0 | (0.0) | 2 | (6.5) | 1 | (4.8) | 2 | (4.3) | 1 | (2.4) | 2 | (3.5) | 1 | (3.7) |
| discontinued due to a serious adverse event | 2 | (6.3) | 0 | (0.0) | 1 | (3.2) | 1 | (4.8) | 2 | (4.3) | 1 | (2.4) | 3 | (5.3) | 1 | (3.7) |



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## 付録 2.7.4-135 有害事象の要約（男女別）

### 001 試験パート B2+D（APaT 集団）（続き）

| | Total | | | |
|---|---|---|---|---|
| | Male | | Female | |
| | n | (%) | n | (%) |
| Patients in population | 167 | | 109 | |
| with one or more adverse events | 164 | (98.2) | 108 | (99.1) |
| with no adverse event | 3 | (1.8) | 1 | (0.9) |
| with drug-related[†] adverse events | 144 | (86.2) | 92 | (84.4) |
| with Grade 3- 5 adverse events | 73 | (43.7) | 45 | (41.3) |
| with Grade 3- 5 drug-related adverse events | 26 | (15.6) | 13 | (11.9) |
| with serious adverse events | 56 | (33.5) | 36 | (33.0) |
| with serious drug-related adverse events | 14 | (8.4) | 8 | (7.3) |
| who died | 0 | (0.0) | 0 | (0.0) |
| with drug-related death | 0 | (0.0) | 0 | (0.0) |
| discontinued[‡] due to an adverse event | 12 | (7.2) | 10 | (9.2) |
| discontinued due to a drug-related adverse event | 7 | (4.2) | 3 | (2.8) |
| discontinued due to a serious adverse event | 8 | (4.8) | 3 | (2.8) |



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## 付録 2.7.4-135 有害事象の要約（男女別）

## 001 試験パート B2+D（APaT 集団）（続き）

| | Ipi-naïve 2 mg/kg Q3W | | | | Ipi-naïve 10 mg/kg Q3W | | | | Ipi-exposed 2 mg/kg Q3W | | | | Ipi-exposed 10 mg/kg Q3W | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Male | | Female | | Male | | Female | | Male | | Female | | Male | | Female | |
| | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) |
| discontinued due to a serious drug-related adverse event | 1 | (3.1) | 0 | (0.0) | 1 | (3.2) | 0 | (0.0) | 2 | (4.3) | 1 | (2.4) | 1 | (1.8) | 0 | (0.0) |

## 付録 2.7.4-135 有害事象の要約（男女別）

## 001 試験パート B2+D（APaT 集団）（続き）

| | Total | | | |
|---|---|---|---|---|
| | Male | | Female | |
| | n | (%) | n | (%) |
| discontinued due to a serious drug-related adverse event | 5 | (3.0) | 1 | (0.9) |

Grades are based on NCI CTCAE version 4.0.
MedDRA preferred terms ‘Progressive Disease’ and ‘Malignant Neoplasm Progression' not related to the drug are excluded.
[†] Determined by the investigator to be related to the drug.
[‡] Study medication withdrawn.
(Database Cutoff Date: [redacted]

Data Source: [資料5.3.5.2.1.2: P001V02]



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## 付録 2.7.4-136 有害事象の要約（男女別）

### 001 試験パート B3（APaT 集団）

| | MK-3475 10 mg/kg Q3W | | | | MK-3475 10 mg/kg Q2W | | | | Total | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Male | | Female | | Male | | Female | | Male | | Female | |
| | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) |
| Patients in population | 72 | | 49 | | 87 | | 36 | | 159 | | 85 | |
| with one or more adverse events | 69 | (95.8) | 48 | (98.0) | 87 | (100.0) | 36 | (100.0) | 156 | (98.1) | 84 | (98.8) |
| with no adverse event | 3 | (4.2) | 1 | (2.0) | 0 | (0.0) | 0 | (0.0) | 3 | (1.9) | 1 | (1.2) |
| with drug-related[†] adverse events | 59 | (81.9) | 40 | (81.6) | 71 | (81.6) | 28 | (77.8) | 130 | (81.8) | 68 | (80.0) |
| with Grade 3- 5 adverse events | 24 | (33.3) | 19 | (38.8) | 39 | (44.8) | 14 | (38.9) | 63 | (39.6) | 33 | (38.8) |
| with Grade 3- 5 drug-related adverse events | 10 | (13.9) | 4 | (8.2) | 15 | (17.2) | 4 | (11.1) | 25 | (15.7) | 8 | (9.4) |
| with serious adverse events | 16 | (22.2) | 12 | (24.5) | 30 | (34.5) | 8 | (22.2) | 46 | (28.9) | 20 | (23.5) |
| with serious drug-related adverse events | 6 | (8.3) | 2 | (4.1) | 10 | (11.5) | 2 | (5.6) | 16 | (10.1) | 4 | (4.7) |
| who died | 2 | (2.8) | 0 | (0.0) | 1 | (1.1) | 0 | (0.0) | 3 | (1.9) | 0 | (0.0) |
| with drug-related death | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) |
| discontinued[‡] due to an adverse event | 7 | (9.7) | 4 | (8.2) | 12 | (13.8) | 5 | (13.9) | 19 | (11.9) | 9 | (10.6) |
| discontinued due to a drug-related adverse event | 1 | (1.4) | 0 | (0.0) | 3 | (3.4) | 1 | (2.8) | 4 | (2.5) | 1 | (1.2) |
| discontinued due to a serious adverse event | 5 | (6.9) | 2 | (4.1) | 8 | (9.2) | 4 | (11.1) | 13 | (8.2) | 6 | (7.1) |
| discontinued due to a serious drug-related adverse event | 1 | (1.4) | 0 | (0.0) | 2 | (2.3) | 1 | (2.8) | 3 | (1.9) | 1 | (1.2) |

Grades are based on NCI CTCAE version 4.0.
MedDRA preferred terms ‘Progressive Disease’ and ‘Malignant Neoplasm Progression' not related to the drug are excluded.
[†] Determined by the investigator to be related to the drug.
[‡] Study medication withdrawn.
(Database Cutoff Date: [redacted]

Data Source: [資料5.3.5.2.1.2: P001V02]



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## 付録 2.7.4-137 有害事象の要約（地域別）

## 001 試験パート B2+D（APaT 集団）

| | Ipi-naïve 2 mg/kg Q3W | | | | Ipi-naïve 10 mg/kg Q3W | | | | Ipi-exposed 2 mg/kg Q3W | | | | Ipi-exposed 10 mg/kg Q3W | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | US | | Ex-US | | US | | Ex-US | | US | | Ex-US | | US | | Ex-US | |
| | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) |
| Patients in population | 30 | | 21 | | 29 | | 23 | | 70 | | 19 | | 61 | | 23 | |
| with one or more adverse events | 30 | (100.0) | 21 | (100.0) | 28 | (96.6) | 23 | (100.0) | 69 | (98.6) | 19 | (100.0) | 59 | (96.7) | 23 | (100.0) |
| with no adverse event | 0 | (0.0) | 0 | (0.0) | 1 | (3.4) | 0 | (0.0) | 1 | (1.4) | 0 | (0.0) | 2 | (3.3) | 0 | (0.0) |
| with drug-related[†] adverse events | 26 | (86.7) | 18 | (85.7) | 25 | (86.2) | 22 | (95.7) | 56 | (80.0) | 19 | (100.0) | 50 | (82.0) | 20 | (87.0) |
| with Grade 3- 5 adverse events | 12 | (40.0) | 7 | (33.3) | 16 | (55.2) | 6 | (26.1) | 29 | (41.4) | 8 | (42.1) | 30 | (49.2) | 10 | (43.5) |
| with Grade 3- 5 drug-related adverse events | 7 | (23.3) | 5 | (23.8) | 1 | (3.4) | 1 | (4.3) | 11 | (15.7) | 4 | (21.1) | 10 | (16.4) | 0 | (0.0) |
| with serious adverse events | 7 | (23.3) | 7 | (33.3) | 11 | (37.9) | 7 | (30.4) | 23 | (32.9) | 4 | (21.1) | 24 | (39.3) | 9 | (39.1) |
| with serious drug-related adverse events | 4 | (13.3) | 3 | (14.3) | 0 | (0.0) | 3 | (13.0) | 7 | (10.0) | 0 | (0.0) | 4 | (6.6) | 1 | (4.3) |
| who died | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) |
| with drug-related death | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) |
| discontinued[‡] due to an adverse event | 1 | (3.3) | 1 | (4.8) | 1 | (3.4) | 4 | (17.4) | 3 | (4.3) | 2 | (10.5) | 7 | (11.5) | 3 | (13.0) |
| discontinued due to a drug-related adverse event | 0 | (0.0) | 1 | (4.8) | 0 | (0.0) | 3 | (13.0) | 3 | (4.3) | 0 | (0.0) | 3 | (4.9) | 0 | (0.0) |
| discontinued due to a serious adverse event | 1 | (3.3) | 1 | (4.8) | 1 | (3.4) | 1 | (4.3) | 3 | (4.3) | 0 | (0.0) | 4 | (6.6) | 0 | (0.0) |



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## 付録 2.7.4-137 有害事象の要約（地域別）

## 001 試験パート B2+D（APaT 集団）（続き）

| | Total | | | |
|---|---|---|---|---|
| | US | | Ex-US | |
| | n | (%) | n | (%) |
| Patients in population | 190 | | 86 | |
| with one or more adverse events | 186 | (97.9) | 86 | (100.0) |
| with no adverse event | 4 | (2.1) | 0 | (0.0) |
| with drug-related[†] adverse events | 157 | (82.6) | 79 | (91.9) |
| with Grade 3- 5 adverse events | 87 | (45.8) | 31 | (36.0) |
| with Grade 3- 5 drug-related adverse events | 29 | (15.3) | 10 | (11.6) |
| with serious adverse events | 65 | (34.2) | 27 | (31.4) |
| with serious drug-related adverse events | 15 | (7.9) | 7 | (8.1) |
| who died | 0 | (0.0) | 0 | (0.0) |
| with drug-related death | 0 | (0.0) | 0 | (0.0) |
| discontinued[‡] due to an adverse event | 12 | (6.3) | 10 | (11.6) |
| discontinued due to a drug-related adverse event | 6 | (3.2) | 4 | (4.7) |
| discontinued due to a serious adverse event | 9 | (4.7) | 2 | (2.3) |



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## 付録 2.7.4-137 有害事象の要約（地域別）

## 001 試験パート B2+D（APaT 集団）（続き）

| | Ipi-naïve 2 mg/kg Q3W | | | | Ipi-naïve 10 mg/kg Q3W | | | | Ipi-exposed 2 mg/kg Q3W | | | | Ipi-exposed 10 mg/kg Q3W | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | US | | Ex-US | | US | | Ex-US | | US | | Ex-US | | US | | Ex-US | |
| | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) |
| discontinued due to a serious drug-related adverse event | 0 | (0.0) | 1 | (4.8) | 0 | (0.0) | 1 | (4.3) | 3 | (4.3) | 0 | (0.0) | 1 | (1.6) | 0 | (0.0) |

## 付録 2.7.4-137 有害事象の要約（地域別）

## 001 試験パート B2+D（APaT 集団）（続き）

| | Total | | | |
|---|---|---|---|---|
| | US | | Ex-US | |
| | n | (%) | n | (%) |
| discontinued due to a serious drug-related adverse event | 4 | (2.1) | 2 | (2.3) |

Grades are based on NCI CTCAE version 4.0.
MedDRA preferred terms ‘Progressive Disease’ and ‘Malignant Neoplasm Progression' not related to the drug are excluded.
† Determined by the investigator to be related to the drug.
‡ Study medication withdrawn.
(Database Cutoff Date: [redacted]

Data Source: [資料5.3.5.2.1.2: P001V02]



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## 付録 2.7.4-138 有害事象の要約（地域別）

## 001 試験パート B3（APaT 集団）

| | MK-3475 10 mg/kg Q3W | | | | MK-3475 10 mg/kg Q2W | | | | Total | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | US | | Ex-US | | US | | Ex-US | | US | | Ex-US | |
| | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) |
| Patients in population | 91 | | 30 | | 97 | | 26 | | 188 | | 56 | |
| with one or more adverse events | 87 | (95.6) | 30 | (100.0) | 97 | (100.0) | 26 | (100.0) | 184 | (97.9) | 56 | (100.0) |
| with no adverse event | 4 | (4.4) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 4 | (2.1) | 0 | (0.0) |
| with drug-related† adverse events | 74 | (81.3) | 25 | (83.3) | 76 | (78.4) | 23 | (88.5) | 150 | (79.8) | 48 | (85.7) |
| with Grade 3- 5 adverse events | 33 | (36.3) | 10 | (33.3) | 45 | (46.4) | 8 | (30.8) | 78 | (41.5) | 18 | (32.1) |
| with Grade 3- 5 drug-related adverse events | 9 | (9.9) | 5 | (16.7) | 18 | (18.6) | 1 | (3.8) | 27 | (14.4) | 6 | (10.7) |
| with serious adverse events | 19 | (20.9) | 9 | (30.0) | 34 | (35.1) | 4 | (15.4) | 53 | (28.2) | 13 | (23.2) |
| with serious drug-related adverse events | 3 | (3.3) | 5 | (16.7) | 11 | (11.3) | 1 | (3.8) | 14 | (7.4) | 6 | (10.7) |
| who died | 1 | (1.1) | 1 | (3.3) | 1 | (1.0) | 0 | (0.0) | 2 | (1.1) | 1 | (1.8) |
| with drug-related death | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) |
| discontinued‡ due to an adverse event | 6 | (6.6) | 5 | (16.7) | 13 | (13.4) | 4 | (15.4) | 19 | (10.1) | 9 | (16.1) |
| discontinued due to a drug-related adverse event | 1 | (1.1) | 0 | (0.0) | 4 | (4.1) | 0 | (0.0) | 5 | (2.7) | 0 | (0.0) |
| discontinued due to a serious adverse event | 5 | (5.5) | 2 | (6.7) | 10 | (10.3) | 2 | (7.7) | 15 | (8.0) | 4 | (7.1) |
| discontinued due to a serious drug-related adverse event | 1 | (1.1) | 0 | (0.0) | 3 | (3.1) | 0 | (0.0) | 4 | (2.1) | 0 | (0.0) |

Grades are based on NCI CTCAE version 4.0.
MedDRA preferred terms 'Progressive Disease' and 'Malignant Neoplasm Progression' not related to the drug are excluded.
† Determined by the investigator to be related to the drug.
‡ Study medication withdrawn.
(Database Cutoff Date: [redacted]

Data Source: [資料5.3.5.2.1.2: P001V02]



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## 付録 2.7.4-139 有害事象の MedDRA 基本語一覧

| 器官別大分類 | 基本語 | 重篤 | 非重篤 | 総数 |
|---|---|---|---|---|
| 血液およびリンパ系障害 | 抗第ＶＩＩＩ因子、抗第ＸＩ因子、または抗第ＸＩＩＩ因子を有する後天性血友病 | 1 | 0 | 1 |
| | 貧血 | 1 | 5 | 6 |
| | 溶血性貧血 | 1 | 0 | 1 |
| | 鉄欠乏性貧血 | 1 | 0 | 1 |
| | リンパ節症 | 1 | 1 | 2 |
| | 好中球減少症 | 0 | 2 | 2 |
| | 汎血球減少症 | 1 | 0 | 1 |
| | 血小板減少症 | 0 | 3 | 3 |
| | 血小板増加症 | 0 | 1 | 1 |
| 心臓障害 | 心房細動 | 1 | 0 | 1 |
| | 心停止 | 2 | 0 | 2 |
| | 心筋炎 | 0 | 1 | 1 |
| | 動悸 | 0 | 1 | 1 |
| 耳および迷路障害 | 難聴 | 1 | 0 | 1 |
| 内分泌障害 | 副腎機能不全 | 0 | 1 | 1 |
| | 悪性腫瘍に伴う高カルシウム血症 | 1 | 0 | 1 |
| | 甲状腺機能亢進症 | 1 | 0 | 1 |
| | 男性性腺機能低下 | 1 | 0 | 1 |
| | 下垂体炎 | 0 | 3 | 3 |
| | 下垂体機能低下症 | 0 | 2 | 2 |
| | 甲状腺機能低下症 | 1 | 5 | 6 |
| | 続発性副腎皮質機能不全 | 1 | 0 | 1 |
| | 甲状腺炎 | 1 | 0 | 1 |
| 眼障害 | 複視 | 0 | 1 | 1 |
| | 黄斑症 | 1 | 0 | 1 |
| | 網膜剥離 | 0 | 1 | 1 |
| | 網膜出血 | 0 | 1 | 1 |
| | 網膜下液 | 1 | 0 | 1 |
| | ぶどう膜炎 | 1 | 1 | 2 |
| | 霧視 | 0 | 3 | 3 |
| | 視力障害 | 1 | 2 | 3 |



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## 付録 2.7.4-139 有害事象の MedDRA 基本語一覧（続き）

| 器官別大分類 | 基本語 | 重篤 | 非重篤 | 総数 |
|---|---|---|---|---|
| 胃腸障害 | 腹部不快感 | 0 | 1 | 1 |
| | 腹痛 | 0 | 4 | 4 |
| | 上腹部痛 | 1 | 0 | 1 |
| | 口唇炎 | 0 | 1 | 1 |
| | 大腸炎 | 0 | 4 | 4 |
| | 潰瘍性大腸炎 | 0 | 1 | 1 |
| | 便秘 | 0 | 2 | 2 |
| | 下痢 | 1 | 11 | 12 |
| | 口内乾燥 | 0 | 3 | 3 |
| | 消化不良 | 0 | 1 | 1 |
| | 嚥下障害 | 1 | 1 | 2 |
| | 心窩部不快感 | 1 | 0 | 1 |
| | 放屁 | 0 | 1 | 1 |
| | 排便回数増加 | 0 | 1 | 1 |
| | 胃炎 | 1 | 0 | 1 |
| | 吐血 | 1 | 0 | 1 |
| | 血便排泄 | 0 | 1 | 1 |
| | 腸閉塞 | 2 | 0 | 2 |
| | 機械的イレウス | 0 | 1 | 1 |
| | 悪心 | 4 | 8 | 12 |
| | 膵炎 | 2 | 0 | 2 |
| | 急性膵炎 | 1 | 0 | 1 |
| | 唾液腺腫瘤 | 0 | 1 | 1 |
| | 舌変色 | 0 | 1 | 1 |
| | 嘔吐 | 2 | 4 | 6 |



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## 付録 2.7.4-139 有害事象の MedDRA 基本語一覧（続き）

| 器官別大分類 | 基本語 | 重篤 | 非重篤 | 総数 |
|---|---|---|---|---|
| 一般・全身障害および投与部位の状態 | 歩行不能 | 1 | 0 | 1 |
| | 医薬品副作用 | 1 | 0 | 1 |
| | 有害事象 | 8 | 7 | 15 |
| | 無力症 | 2 | 4 | 6 |
| | 胸部不快感 | 0 | 1 | 1 |
| | 胸痛 | 0 | 2 | 2 |
| | 悪寒 | 0 | 5 | 5 |
| | 状態悪化 | 0 | 1 | 1 |
| | 死亡 | 38 | 0 | 38 |
| | 疾患合併症 | 1 | 0 | 1 |
| | 疾患進行 | 3 | 6 | 9 |
| | 薬効欠如 | 0 | 11 | 11 |
| | 疲労 | 4 | 19 | 23 |
| | 異常感 | 0 | 3 | 3 |
| | 歩行障害 | 2 | 0 | 2 |
| | 全身健康状態低下 | 2 | 3 | 5 |
| | 注入部位血管外漏出 | 0 | 1 | 1 |
| | 注射部位硬結 | 0 | 1 | 1 |
| | 注射部位腫瘤 | 0 | 1 | 1 |
| | 限局性浮腫 | 1 | 0 | 1 |
| | 倦怠感 | 3 | 5 | 8 |
| | 粘膜の炎症 | 0 | 1 | 1 |
| | 有害事象なし | 0 | 21 | 21 |
| | 治療効果なし | 0 | 1 | 1 |
| | 末梢性浮腫 | 0 | 2 | 2 |
| | 疼痛 | 2 | 9 | 11 |
| | 末梢腫脹 | 0 | 1 | 1 |
| | 製品品質の問題 | 0 | 1 | 1 |
| | 発熱 | 1 | 8 | 9 |
| | 腫脹 | 1 | 0 | 1 |
| | 圧痛 | 0 | 1 | 1 |
| | 終末期状態 | 1 | 0 | 1 |
| | 予想外の治療反応 | 0 | 3 | 3 |



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## 付録 2.7.4-139 有害事象の MedDRA 基本語一覧（続き）

| 器官別大分類 | 基本語 | 重篤 | 非重篤 | 総数 |
|---|---|---|---|---|
| 一般・全身障害および投与部位の状態 | 治療レスポンダー | 0 | 1 | 1 |
| | 評価不能の事象 | 0 | 1 | 1 |
| 肝胆道系障害 | 自己免疫性肝炎 | 1 | 1 | 2 |
| | 胆汁うっ滞性肝損傷 | 1 | 0 | 1 |
| | 肝不全 | 1 | 0 | 1 |
| | 急性肝炎 | 1 | 0 | 1 |
| | 高ビリルビン血症 | 0 | 1 | 1 |
| | 黄疸 | 1 | 0 | 1 |
| 免疫系障害 | 自己免疫障害 | 0 | 1 | 1 |
| | サイトカインストーム | 0 | 1 | 1 |
| | 薬物過敏症 | 1 | 0 | 1 |
| | 免疫反応 | 1 | 0 | 1 |
| | 季節性アレルギー | 0 | 1 | 1 |
| 感染症および寄生虫症 | 細菌感染 | 1 | 1 | 2 |
| | カンジダ感染 | 0 | 1 | 1 |
| | クロストリジウム性大腸炎 | 0 | 1 | 1 |
| | クロストリジウム・ディフィシレ大腸炎 | 1 | 0 | 1 |
| | 結腸膿瘍 | 1 | 0 | 1 |
| | 憩室炎 | 1 | 0 | 1 |
| | 歯肉炎 | 0 | 1 | 1 |
| | 帯状疱疹 | 0 | 2 | 2 |
| | 感染 | 2 | 0 | 2 |
| | 鼻咽頭炎 | 0 | 1 | 1 |
| | 口腔感染 | 0 | 1 | 1 |
| | 肺炎 | 2 | 0 | 2 |
| | 敗血症 | 4 | 0 | 4 |
| | 副鼻腔炎 | 0 | 1 | 1 |
| | 尿路感染 | 2 | 1 | 3 |



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## 付録 2.7.4-139 有害事象の MedDRA 基本語一覧（続き）

| 器官別大分類 | 基本語 | 重篤 | 非重篤 | 総数 |
|---|---|---|---|---|
| 傷害、中毒および処置合併症 | 偶発的製品曝露 | 0 | 1 | 1 |
| | 禁忌薬剤投与 | 0 | 1 | 1 |
| | 薬剤誤投与 | 0 | 3 | 3 |
| | 投薬欠落 | 0 | 7 | 7 |
| | 処方過誤 | 0 | 2 | 2 |
| | 焼痂 | 0 | 1 | 1 |
| | 転倒 | 1 | 0 | 1 |
| | 大腿骨骨折 | 1 | 0 | 1 |
| | 不適切な投与計画での薬剤の投与 | 0 | 1 | 1 |
| | 誤った投与期間 | 0 | 1 | 1 |
| | 製品の誤った保存 | 0 | 3 | 3 |
| | 誤った投与経路 | 0 | 2 | 2 |
| | 筋損傷 | 1 | 0 | 1 |
| | 適応外使用 | 0 | 30 | 30 |
| | 品質不良薬剤の投与 | 0 | 1 | 1 |
| | 処置後合併症 | 0 | 1 | 1 |
| | 処置後出血 | 1 | 0 | 1 |
| | 製品使用の問題 | 0 | 1 | 1 |
| | 腱断裂 | 0 | 1 | 1 |
| | 創部分泌 | 1 | 0 | 1 |
| | 薬剤使用過程における誤った技法 | 0 | 7 | 7 |



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## 付録 2.7.4-139 有害事象の MedDRA 基本語一覧（続き）

| 器官別大分類 | 基本語 | 重篤 | 非重篤 | 総数 |
|---|---|---|---|---|
| 臨床検査 | アラニンアミノトランスフェラーゼ異常 | 1 | 0 | 1 |
| | アラニンアミノトランスフェラーゼ増加 | 0 | 1 | 1 |
| | アミラーゼ増加 | 0 | 1 | 1 |
| | アスパラギン酸アミノトランスフェラーゼ増加 | 0 | 1 | 1 |
| | 血中ビリルビン増加 | 1 | 1 | 2 |
| | 血中コレステロール増加 | 0 | 1 | 1 |
| | 血中クレアチンホスホキナーゼＭＢ増加 | 0 | 1 | 1 |
| | 血中クレアチニン増加 | 2 | 0 | 2 |
| | 血中ブドウ糖増加 | 3 | 0 | 3 |
| | 血中乳酸脱水素酵素減少 | 0 | 1 | 1 |
| | 血中乳酸脱水素酵素増加 | 0 | 2 | 2 |
| | 酵素濃度増加 | 1 | 0 | 1 |
| | 心拍数増加 | 1 | 0 | 1 |
| | 肝酵素上昇 | 1 | 4 | 5 |
| | リパーゼ増加 | 0 | 3 | 3 |
| | 肝機能検査異常 | 1 | 1 | 2 |
| | 心筋壊死マーカー上昇 | 0 | 1 | 1 |
| | 血小板数異常 | 0 | 2 | 2 |
| | 血小板数減少 | 1 | 0 | 1 |
| | ＰＯ２低下 | 1 | 0 | 1 |
| | ブドウ球菌検査陽性 | 0 | 1 | 1 |
| | トランスアミナーゼ上昇 | 1 | 0 | 1 |
| | 体重減少 | 1 | 3 | 4 |



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## 付録 2.7.4-139 有害事象の MedDRA 基本語一覧（続き）

| 器官別大分類 | 基本語 | 重篤 | 非重篤 | 総数 |
|---|---|---|---|---|
| 代謝および栄養障害 | 食欲減退 | 2 | 5 | 7 |
| | 脱水 | 1 | 0 | 1 |
| | 糖尿病性ケトアシドーシス | 2 | 0 | 2 |
| | 成長障害 | 1 | 0 | 1 |
| | 栄養補給障害 | 0 | 2 | 2 |
| | 高血糖 | 0 | 1 | 1 |
| | 低カリウム血症 | 1 | 0 | 1 |
| | 低ナトリウム血症 | 1 | 1 | 2 |
| | 低リン酸血症 | 1 | 0 | 1 |
| | 血液量減少症 | 0 | 1 | 1 |
| | ケトアシドーシス | 1 | 0 | 1 |
| | 腫瘍崩壊症候群 | 1 | 0 | 1 |
| 筋骨格系および結合組織障害 | 関節痛 | 1 | 9 | 10 |
| | 関節炎 | 1 | 0 | 1 |
| | 腋窩腫瘤 | 0 | 1 | 1 |
| | 骨痛 | 0 | 1 | 1 |
| | 側腹部痛 | 0 | 1 | 1 |
| | 椎間板障害 | 1 | 0 | 1 |
| | 関節硬直 | 0 | 1 | 1 |
| | 関節腫脹 | 0 | 2 | 2 |
| | 筋力低下 | 0 | 3 | 3 |
| | 筋骨格痛 | 0 | 1 | 1 |
| | 筋骨格硬直 | 0 | 1 | 1 |
| | 筋肉痛 | 2 | 5 | 7 |
| | 四肢痛 | 0 | 1 | 1 |
| | 関節リウマチ | 1 | 0 | 1 |
| | 軟部組織壊死 | 1 | 0 | 1 |
| | 変形性脊椎症 | 0 | 1 | 1 |



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## 付録 2.7.4-139 有害事象の MedDRA 基本語一覧（続き）

| 器官別大分類 | 基本語 | 重篤 | 非重篤 | 総数 |
|---|---|---|---|---|
| 良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） | 骨新生物 | 0 | 1 | 1 |
| | 脳新生物 | 0 | 1 | 1 |
| | 脳の悪性新生物 | 1 | 0 | 1 |
| | 癌、寛解期 | 0 | 1 | 1 |
| | 癌疼痛 | 1 | 1 | 2 |
| | 悪性黒色腫 | 1 | 0 | 1 |
| | 悪性黒色腫第４期 | 1 | 0 | 1 |
| | 悪性新生物進行 | 44 | 3 | 47 |
| | 再発黒色腫 | 2 | 0 | 2 |
| | 中枢神経系転移 | 3 | 0 | 3 |
| | 遠隔転移を伴う悪性黒色腫 | 5 | 0 | 5 |
| | 遠隔転移を伴う眼球黒色腫 | 1 | 0 | 1 |
| | 新生物 | 1 | 1 | 2 |
| | 悪性新生物 | 1 | 0 | 1 |
| | 新生物進行 | 1 | 0 | 1 |



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## 付録 2.7.4-139 有害事象の MedDRA 基本語一覧（続き）

| 器官別大分類 | 基本語 | 重篤 | 非重篤 | 総数 |
|---|---|---|---|---|
| 神経系障害 | 健忘 | 0 | 1 | 1 |
| | 平衡障害 | 1 | 1 | 2 |
| | 脳浮腫 | 2 | 0 | 2 |
| | 灼熱感 | 0 | 1 | 1 |
| | 中枢神経系出血 | 1 | 0 | 1 |
| | 出血 | 0 | 1 | 1 |
| | 中枢神経系病変 | 2 | 0 | 2 |
| | 脳出血 | 1 | 0 | 1 |
| | 昏睡 | 1 | 0 | 1 |
| | 浮動性めまい | 0 | 1 | 1 |
| | 統合運動障害 | 0 | 1 | 1 |
| | 起立障害 | 0 | 1 | 1 |
| | 顔面不全麻痺 | 2 | 0 | 2 |
| | 頭痛 | 1 | 5 | 6 |
| | 片頭痛 | 0 | 1 | 1 |
| | 重症筋無力症 | 2 | 0 | 2 |
| | 筋無力症候群 | 1 | 0 | 1 |
| | 神経系障害 | 1 | 0 | 1 |
| | 末梢性ニューロパチー | 0 | 1 | 1 |
| | 視神経炎 | 0 | 1 | 1 |
| | 部分発作 | 0 | 1 | 1 |
| | 痙攣発作 | 3 | 0 | 3 |
| | 会話障害 | 0 | 1 | 1 |
| | 振戦 | 1 | 1 | 2 |
| | 刺激無反応 | 1 | 0 | 1 |



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## 付録 2.7.4-139 有害事象の MedDRA 基本語一覧（続き）

| 器官別大分類 | 基本語 | 重篤 | 非重篤 | 総数 |
|---|---|---|---|---|
| 精神障害 | 異常行動 | 0 | 1 | 1 |
| | 激越 | 1 | 0 | 1 |
| | 錯乱状態 | 1 | 1 | 2 |
| | 譫妄 | 2 | 0 | 2 |
| | うつ病 | 0 | 1 | 1 |
| | 恐怖 | 0 | 1 | 1 |
| | 感情の平板化 | 0 | 1 | 1 |
| | 不眠症 | 0 | 1 | 1 |
| | 精神状態変化 | 1 | 0 | 1 |
| | 落ち着きのなさ | 1 | 0 | 1 |
| 腎および尿路障害 | 急性腎不全 | 1 | 0 | 1 |
| | 腎炎 | 1 | 1 | 2 |
| | 頻尿 | 0 | 1 | 1 |
| | 腎不全 | 1 | 0 | 1 |
| | 尿閉 | 3 | 0 | 3 |
| 生殖系および乳房障害 | 精巣腫脹 | 0 | 1 | 1 |
| 呼吸器、胸郭および縦隔障害 | 慢性閉塞性肺疾患 | 0 | 2 | 2 |
| | 咳嗽 | 0 | 2 | 2 |
| | 発声障害 | 0 | 1 | 1 |
| | 呼吸困難 | 4 | 2 | 6 |
| | 労作性呼吸困難 | 0 | 1 | 1 |
| | 肺障害 | 1 | 1 | 2 |
| | 鼻閉 | 0 | 1 | 1 |
| | 閉塞性気道障害 | 1 | 0 | 1 |
| | 起坐呼吸 | 0 | 1 | 1 |
| | 胸水 | 0 | 1 | 1 |
| | 肺臓炎 | 2 | 6 | 8 |
| | 肺塞栓症 | 1 | 0 | 1 |
| | 呼吸障害 | 2 | 0 | 2 |
| | 鼻漏 | 0 | 1 | 1 |



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## 付録 2.7.4-139 有害事象の MedDRA 基本語一覧（続き）

| 器官別大分類 | 基本語 | 重篤 | 非重篤 | 総数 |
|---|---|---|---|---|
| 皮膚および皮下組織障害 | 皮膚炎 | 0 | 1 | 1 |
| | 皮膚乾燥 | 0 | 2 | 2 |
| | 紅斑 | 0 | 4 | 4 |
| | 毛髪変色 | 0 | 3 | 3 |
| | 光線過敏性反応 | 0 | 1 | 1 |
| | そう痒症 | 1 | 4 | 5 |
| | 全身性そう痒症 | 0 | 3 | 3 |
| | 乾癬 | 0 | 1 | 1 |
| | 発疹 | 1 | 9 | 10 |
| | 紅斑性皮疹 | 0 | 1 | 1 |
| | 全身性皮疹 | 0 | 2 | 2 |
| | 斑状丘疹状皮疹 | 0 | 1 | 1 |
| | そう痒性皮疹 | 0 | 1 | 1 |
| | 痂皮 | 0 | 1 | 1 |
| | 皮膚変色 | 2 | 0 | 2 |
| | 皮膚障害 | 0 | 1 | 1 |
| | 皮膚病変 | 0 | 1 | 1 |
| | 皮膚熱感 | 0 | 1 | 1 |
| | 蕁麻疹 | 0 | 3 | 3 |
| | 尋常性白斑 | 0 | 1 | 1 |



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## 付録 2.7.4-139 有害事象の MedDRA 基本語一覧（続き）

| 器官別大分類 | 基本語 | 重篤 | 非重篤 | 総数 |
|---|---|---|---|---|
| 外科および内科処置 | 透析 | 1 | 0 | 1 |
| | 入院 | 1 | 0 | 1 |
| | 血小板輸血 | 0 | 1 | 1 |
| | 治療的塞栓術 | 1 | 0 | 1 |
| | 輸血 | 0 | 2 | 2 |
| 血管障害 | 深部静脈血栓症 | 1 | 0 | 1 |
| | 潮紅 | 0 | 1 | 1 |
| | 出血 | 0 | 1 | 1 |
| | 低血圧 | 1 | 0 | 1 |
| | リンパ浮腫 | 1 | 1 | 2 |
| | 起立性低血圧 | 0 | 1 | 1 |
| | 血栓症 | 1 | 0 | 1 |
| 合計 | | 283 | 442 | 725 |
| MedDRA version 18.0にて集計 | | | | |



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