第5部　臨床試験報告書

5.2　全臨床試験一覧表

資料番号	資料表題	著者	実施期間 (FSE to CSR)	試験実施場所	評価・参考
5.2	Tabular Listing of All Clinical Studies	—	—	—	—

5.3　臨床試験報告書

5.3.1　生物薬剤学試験報告書

5.3.1.2　比較BA試験及び生物学的同等性(BE)試験報告書

資料番号	資料表題	著者	実施期間 (FSE to CSR) (月／日／年)	試験実施場所	評価・参考
5.3.1.2-1	Study 20110168 - An Open-label, Randomized, Parallel Study in Healthy Volunteers to Compare the Pharmacokinetics of AMG 145 When Delivered Subcutaneously via a 3.5 mL Personal Injector versus 3 Prefilled Autoinjector/Pens	Amgen	[redacted]	This study was carried out by 4 investigators at 4 centers in the United States	評価
5.3.1.2-2	Study 20120133 - An Open-label, Randomized, Crossover Study in Healthy Volunteers to Compare the Pharmacokinetics of AMG 145 When Delivered Subcutaneously via a Prefilled Syringe Versus a Prefilled Autoinjector/pen	Amgen	[redacted]	This study was conducted at 3 centers in the United States.	評価

5.3.1.4　生物学的及び理化学的分析法検討報告書

資料番号	資料表題	著者	実施期間 (FSE to CSR) (月／日／年)	試験実施場所	評価・参考
5.3.1.4-1	Study 112777 Final Report - Method Qualification of an ELISA for the Quantification of PCSK9 in Human Serum or Plasma	[redacted]	[redacted]	Amgen	評価
5.3.1.4-2	Study 113215 ([redacted]-JFV2) Final Report - Method Transfer Validation of an ELISA for the Quantification of PCSK9 in Human Serum	[redacted]	[redacted]	[redacted]	評価
5.3.1.4-3	Study 112602 Final Report - Method Validation of an ELISA for the Quantification of AMG 145 in Human Serum	[redacted]	[redacted]	Amgen	評価

5.3.1.4-4	Study 113216 ([redacted]-IFV2) Final Report - Method Transfer Validation of an ELISA for the Quantification of AMG 145 in Human Serum	[redacted]	[redacted]-[redacted]	[redacted]	評価
5.3.1.4-5	Study 117093 ([redacted] 12253) Final Report - Quantification of AMG 145 in Human Serum by ELISA	[redacted]	[redacted]-[redacted]	[redacted], India	評価
5.3.1.4-6	Study 117094 ([redacted] 11254) Final Report - Quantification of PCSK9 in Human Serum by ELISA	[redacted]	[redacted]-[redacted]	[redacted], India	評価
5.3.1.4-7	Method MET-002468 An Electrochemiluminescence Immunoassay for the Detection of Antibodies Against AMG 145 in Human Serum using the MSD Sector Imager 6000	[redacted]	[redacted](Report Date)	Amgen	評価
5.3.1.4-8	Method Validation MVR-000352 Analytical Method Validation Report for an Electrochemiluminescence Immunoassay for the Detection of Antibodies Against AMG 145 in Human Serum using the MSD Sector Imager 6000	[redacted]	[redacted](Report Date)	Amgen	評価
5.3.1.4-9	MET-002439 A Bioassay for the Detection of Neutralizing Antibodies to AMG 145 in Human Serum	[redacted]	[redacted](Report Date)	Amgen	評価
5.3.1.4-10	MVR-000349 Validation of a Receptor- Ligand Binding Assay for the Detection of Neutralizing Antibodies Against AMG 145 in Human Serum	[redacted]	[redacted] (Report Date)	Amgen	評価
5.3.1.4-11	Method GCL-277 - An electrochemiluminescence immunoassay to detect antibodies against AMG 145 in human serum	[redacted]	[redacted] (Report Date)	Amgen	評価

5.3.3 臨床薬物動態（PK）試験報告書

5.3.3.1 健康被験者におけるPK及び初期忍容性試験報告書

資料番号	資料表題	著者	実施期間 (FSE to CSR) （月／日／年）	試験実施場所	評価・参考
5.3.3.1-1	Study 20120136 - An Open-label, Crossover, PK/PD Study of AMG 145 to Determine the Intra-subject Variability in Healthy Subjects	Amgen	[redacted]	This study was conducted at a single study center in the United States.	評価
5.3.3.1-2	Study 20120135 - An Open-label, Non-randomized Study in Healthy Volunteers to Assess Drug Delivery Performance of the 3.5 mL Personal Injector Using Placebo Buffer	Amgen	[redacted]	This study was conducted at a single center in the United States.	評価
5.3.3.1-3	Study 20110234 - A Randomized, Crossover Study to Evaluate Tolerability of Various SC Infusion Rates of a 3.5 mL Viscous Placebo Buffer in Healthy Subjects	Amgen	[redacted]	This study was conducted at 1 site in the United States.	評価
5.3.3.1-4	Study 20120101 - A Randomized, Crossover Study to Evaluate Tolerability of Various Placebo Formulations With Different Viscosities Administered Subcutaneously via Bolus Injection in Healthy Subjects	Amgen	[redacted]	This study was conducted at 1 site in the United States.	評価

5.3.3.3 内因性要因を検討したPK試験報告書

資料番号	資料表題	著者	実施期間（FSE to CSR） （月／日／年）	試験実施場所	評価・参考
5.3.3.3-1	Study 20120341 - Open-label, Parallel-group Study Evaluating the Pharmacokinetics of AMG 145 in Hepatic-impaired and Healthy Subjects	Amgen	[redacted]	This study was conducted at 3 centers in the United States.	評価
5.3.3.3-2	Study 20140213 - Phase 1, Open-label, Single-dose Study of Evolocumab (AMG 145) Administered Subcutaneously to Subjects With Normal Renal Function or Severe Renal Impairment or End Stage Renal Disease Receiving Hemodialysis	Amgen	[redacted]	This study was conducted at 1 center in the United States	評価

5.3.3.5 ポピュレーションPK試験報告書

資料番号	資料表題	著者	実施期間 (FSE to CSR) (月／日／年)	試験実施場所	評価・参考
5.3.3.5-1	Study 116744 - Pharmacokinetic/Pharmacodynamic (PK/PD) Modeling and Simulation for AMG 145 Phase 1 and Phase 2 Studies	[redacted]	[redacted] (Report Date)	Amgen	評価
5.3.3.5-2	Study 119663 - Population Pharmacokinetic Modeling and Simulation Update for Evolocumab Phase 1, 2, and 3 Studies	[redacted]	–	Amgen	評価
5.3.3.5-3	Study 120037- Population Pharmacokinetic and Exposure Response Modeling and Simulation - An Update incluidng Japanese Phase 1, 2, and 3 studies	[redacted]	[redacted] (Report Date)	Amgen	評価
5.3.3.5-4	Study 117333- Pharmacodynamic Report for pharmacodynamics of Time Averaged Effect on Serum Lipids Following Administration of AMG 145 in studies 20101154 and 20101155	[redacted]	[redacted] (Report Date)	Amgen	評価

5.3.4 臨床薬力学（PD）試験報告書

5.3.4.1 健康被験者におけるPD試験及びPK/PD試験報告書

資料番号	資料表題	著者	実施期間 (FSE to CSR) (月／日／年)	試験実施場所	評価・参考
5.3.4.1-1	Study 20080397 - A Phase 1, Randomized, Double-Blind, Placebo-Controlled, Ascending Single Dose Study to Evaluate the Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of AMG 145 in Healthy Subjects	Amgen	[redacted]-[redacted]	[redacted], US	評価
5.3.4.1-2	Study 20110121 - A Randomized, Double-blind, Placebo-controlled, Single dose Study to Evaluate the Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of AMG 145 in Healthy Japanese Subjects	Amgen	[redacted]-[redacted]	This study was conducted at 1 center in the United States.	評価

5.3.4.2　患者におけるPD試験及びPK/PD試験報告書

資料番号	資料表題	著者	実施期間 (FSE to CSR) （月／日／年）	試験実施場所	評価・参考
5.3.4.2-1	Study 20080398 - A Phase 1, Randomized, Double-Blind, Placebo-Controlled, Ascending Multiple Dose Study to Evaluate the Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of AMG 145 in Subjects with Hyperlipidemia on Stable Doses of a Statin	Amgen	06/28/2010-[redacted]	This study was conducted at 10 sites in the United States.	評価

5.3.5　有効性及び安全性試験報告書

5.3.5A　有効性及び安全性試験報告書（高コレステロール血症及び家族性高コレステロール血症ヘテロ接合体）

5.3.5A.1　申請する適応症に関する比較対照試験報告書（高コレステロール血症及び家族性高コレステロール血症ヘテロ接合体）

資料番号	資料表題	著者	実施期間 (FSE to CSR) （月／日／年）	試験実施場所	評価・参考
5.3.5A.1-1	Study 20101154 - A Randomized, Placebo- and Ezetimibe-controlled, Dose-ranging Study to Evaluate Tolerability and Efficacy of AMG 145 on LDL-C in Hypercholesterolemic Subjects With a 10-year Framingham Risk Score of 10% or Less (MENDEL: Monoclonal antibody against PCSK9 to reduce Elevated LDL-C in subjects currently Not receiving Drug therapy for Easing Lipid levels) Type of Control: placebo	Amgen	07/06/2011-[redacted]	This study was conducted at 52 centers in the United States, Canada, Australia, Belgium, and Denmark.	評価
5.3.5A.1-2	Study 20101155 - LAPLACE -TIMI 57 - A Double-blind, Randomized, Placebo-controlled, Multicenter, Dose-ranging Study to Evaluate Tolerability and Efficacy of AMG 145 on LDL-C in Combination with HMG-CoA Reductase Inhibitors in Hypercholesterolemic Subjects (LAPLACE: LDL-C Assessment w/ PCSK9 monoclonaL Antibody inhibition Combined with statin thErapy) Type of Control = placebo	Amgen	07/18/2011-[redacted]	This study was conducted at 78 centers in the United States, Canada, and Europe.	評価

5.3.5A.1-3	Study 20090158 - A Double-blind, Randomized, Placebo-controlled, Multicenter Study to Evaluate Tolerability and Efficacy of AMG 145 on LDL-C in Subjects with Heterozygous Familial Hypercholesterolemia Type of Control = placebo	Amgen	08/02/2011-[redacted]	This study was conducted at 24 centers in Asia, Canada, Europe, South Africa, and the United States.	評価
5.3.5A.1-4	Study 20090159 - A Randomized, Multicenter Study to Evaluate Tolerability and Efficacy of AMG 145 on LDL-C, Compared with Ezetimibe, in Hypercholesterolemic Subjects Unable to Tolerate an Effective Dose of a HMG-CoA Reductase Inhibitor (GAUSS: Goal Achievement after Utilizing an anti PCSK9 antibody in Statin Intolerant Subjects) Type of Control = placebo	Amgen	[redacted]	This study was conducted at 33 centers in Australia, Belgium, Canada, Denmark, Finland, Spain, Sweden, and the United States.	評価
5.3.5A.1-5	Study 20110114 - A Double-blind, Randomized, Placebo and Ezetimibe-controlled, Multicenter Study to Evaluate Safety and Efficacy of Lipid Lowering Monotherapy With AMG 145 in Subjects With a 10-Year Framingham Risk Score of 10% or Less Type of Control = placebo	Amgen	[redacted]	This study was conducted at 71 centers in the United States of America, Denmark, Belgium, Australia, Canada, France, South Korea, Taiwan, and Turkey.	評価
5.3.5A.1-6	Study 20110115 - A Double-blind, Randomized, Placebo and Ezetimibe Controlled, Multicenter Study to Evaluate Safety, Tolerability and Efficacy of AMG 145 on LDL-C in Combination With Statin Therapy in Subjects With Primary Hypercholesterolemia and Mixed Dyslipidemia Type of Control = placebo	Amgen	[redacted]	This study was conducted at 198 centers in the United States, Czech Republic, United Kingdom, Canada, Denmark, Germany, Russia, Hungary, Italy, Australia, Netherlands, Belgium, Sweden, Switzerland, Spain, France, and Hong Kong.	評価

5.3.5A.1-7	Study 20110116 - A Double-blind, Randomized, Multicenter Study to Evaluate Safety and Efficacy of AMG 145, Compared With Ezetimibe, in Hypercholesterolemic Subjects Unable to Tolerate an Effective Dose of a HMG-CoA Reductase Inhibitor Type of Control = placebo	Amgen	[redacted]	This study was conducted at 51 centers in the United States, Australia, Netherlands, Denmark, Spain, Germany, United Kingdom, Belgium, France, Canada, Switzerland, Hong Kong, and Poland.	評価
5.3.5A.1-8	Study 20110117 - A Double-blind, Randomized, Placebo-controlled, Multicenter Study to Evaluate Safety, Tolerability and Efficacy of AMG 145 on LDL-C in Subjects With Heterozygous Familial Hypercholesterolemia (RUTHERFORD-2) Type of Control = placebo	Amgen	[redacted]	This study was conducted at 39 centers in Canada, Netherlands, South Africa, Spain, United States, Germany, United Kingdom, Norway,Sweden, France, Switzerland, Australia, New Zealand, and Hong Kong.	評価
5.3.5A.1-9	Study 20110109 - A Double-blind, Randomized, Placebo-controlled, Multicenter Study to Evaluate Long-term Tolerability and Durable Efficacy of AMG 145 on LDL-C in Hyperlipidemic Subjects Type of Control = placebo	Amgen	01/05/2012-[redacted]	This study was conducted at 88 study centers in the USA, Canada, South Africa, Czech Republic, Denmark, Hungary, Belgium, Australia, and Austria.	評価
5.3.5A.1-10	Study 20110231 - A Double-blind, Randomized, Placebo-controlled, Multicenter Study to Evaluate Tolerability and Efficacy of AMG 145 on LDL-C in Combination With Stable Statin Therapy in Japanese Subjects With Hypercholesterolemia and High Cardiovascular Risk Type of Control = placebo	Amgen	07/10/2012-[redacted]	This study was conducted at 40 centers in Japan.	評価

5.3.5A.1-11	Study 20120122 -A Double-blind, Randomized, Placebo-controlled, Multicenter Study to Evaluate Safety, Tolerability and Efficacy of Evolocumab (AMG 145) on LDL-C in Combination With Statin Therapy in Japanese Subjects With High Cardiovascular Risk and With Hyperlipidemia or Mixed Dyslipidemia (YUKAWA-2)	Amgen	[redacted]	This study was conducted at 52 centers in Japan.	評価
5.3.5A.1-12	Study 20110110 - A Multicenter, Controlled, Open-label Extension Study to Assess the Long-term Safety and Efficacy of Evolocumab Type of Control = active control without placebo	Amgen	[redacted](ongoing)	This study was conducted at 189 centers in the United States, Europe (11 countries), Japan, Canada, South Africa, Australia, and other countries in the Asia-Pacific region.	評価
5.3.5A.1-13-1 5.3.5A.1-13-2	Study 20120138 - A Multicenter, Controlled, Open-label Extension (OLE) Study to Assess the Long-term Safety and Efficacy of AMG 145 Type of Control = active control without placebo	Amgen	[redacted](ongoing)	This study is being conducted at approximately 450 study centers. This interim analysis included subjects enrolled at 282 centers in the US, Canada, Denmark, Czech Republic, Australia, the United Kingdom, Belgium, Germany, the Netherlands, Hungary, South Africa, Spain, Italy, Sweden, the Russian Federation, France, Switzerland, Norway, Hong Kong, New Zealand, Taiwan, and South Korea.	評価

5.3.5.3 複数の試験成績を併せて解析した報告書

資料番号	資料表題	著者	実施期間 (FSE to CSR) (月／日／年)	試験実施場所	評価・参考
5.3.5.3-1	Integrated Summary of Efficacy (TFL)	[redacted]	—	Amgen	評価
5.3.5.3-2	Integrated Summary of Safety	[redacted]	—	Amgen	評価
5.3.5.3-3	その他の解析	[redacted]	—	Amgen	評価
5.3.5.3-4-1	Integrated Immunogenicity Report1	[redacted]	—	Amgen	評価
5.3.5.3-4-2	Integrated Immunogenicity Report2	[redacted]	[redacted] (Report writing competed)	Amgen	評価

5.3.5A.4　その他の臨床試験報告書（高コレステロール血症及び家族性高コレステロール血症ヘテロ接合体）

資料番号	資料表題	著者	実施期間 (FSE to CSR) （月／日／年）	試験実施場所	評価・参考
5.3.5A.4-1	Study 20120356 - A Multi-Center, Randomized Study in Subjects With Primary Hypercholesterolemia or Mixed Dyslipidemia to Assess Subjects' Ability to Administer a Full Dose of AMG 145 in Home-use, Using Either a 3.5 ml Personal Injector or a Prefilled Autoinjector/Pen	Amgen	[redacted]- [redacted]	This study was conducted at 23 centers in theUnited States of America (USA) and Canada.	評価
5.3.5A.4-2	Study 20120348 - A Multi-center, Randomized Study in Subjects With Primary Hypercholesterolemia or Mixed Dyslipidemia to Assess Subjects' Ability to Administer a Full Dose of AMG 145 in Home-use, Using Either a Prefilled Syringe or a Prefilled Autoinjector/pen	Amgen	04/18/2013- [redacted]	This study was conducted at 22 centers in the United States of America (USA) and Canada.	評価

5.3.5B　有効性及び安全性試験報告書（家族性高コレステロール血症ホモ接合体）

5.3.5B.1　申請する適応症に関する比較対照試験報告書（家族性高コレステロール血症ホモ接合体）

資料番号	資料表題	著者	実施期間 (FSE to CSR) （月／日／年）	試験実施場所	評価・参考
5.3.5B.1-1	Study 20110233 - A 2-Part, Phase 2/3 Study to Assess the Safety, Tolerability and Efficacy of AMG 145 in Subjects With Homozygous Familial Hypercholesterolemia Type of Control = placebo	Amgen	04/05/2012- [redacted]	Phase 2 was conducted at a total of 2 centers in the United States and South Africa. Phase 3 was conducted at a total of 17 centers in South Africa, the Netherlands, the Czech Republic, Spain, Canada, the United States, Belgium, France, Italy, and Lebanon.	評価

5.3.5B.2　非対照試験報告書（家族性高コレステロール血症ホモ接合体）

資料番号	資料表題	著者	実施期間 (FSE to CSR) （月／日／年）	試験実施場所	評価・参考
5.3.5B.2-1	Study 20110271 - A Multicenter, Open-label Study to Assess the Long-term Safety, Tolerability, and Efficacy of AMG 145 on LDL-C in Subjects With Severe Familial Hypercholesterolemia	Amgen	[redacted]- [redacted](ongoing)	As of the data cutoff date ([redacted]) for this interim report, a total of 36 centers in South Africa, the United States, the Czech Republic, France, Canada, Japan, Netherlands, Italy, Spain, New Zealand, the United Kingdom, Belgium, Greece, Australia, and Hong Kong had enrolled subjects.	評価

5.3.7　患者データ一覧表及び症例記録

資料番号	資料表題	著者	実施期間 (FSE to CSR) （月／日／年）	試験実施場所	評価・参考
5.3.1.2-1	患者データ一覧表（Study 20110168）	[redacted]	[redacted]	Amgen	評価
5.3.1.2-2	患者データ一覧表（Study 20120133）	[redacted]	[redacted]	Amgen	評価
5.3.3.1-1	患者データ一覧表（Study 20120136）	[redacted]	[redacted]	Amgen	評価
5.3.3.1-2	患者データ一覧表（Study 20120135）	[redacted]	[redacted]	Amgen	評価
5.3.3.1-3	患者データ一覧表（Study 20110234）	[redacted]	[redacted]	Amgen	評価
5.3.3.1-4	患者データ一覧表（Study 20120101）	[redacted]	[redacted]	Amgen	評価
5.3.3.3-1	患者データ一覧表（Study 20120341）	[redacted]	[redacted]	Amgen	評価
5.3.3.3-2	患者データ一覧表（Study 20140213）	[redacted]	[redacted]	Amgen	評価
5.3.4.1-1	患者データ一覧表（Study 20080397）	[redacted]	[redacted]	Amgen	評価
5.3.4.1-2	患者データ一覧表（Study 20110121）	[redacted]	[redacted]	Amgen	評価
5.3.4.2-1	患者データ一覧表（Study 20080398）	[redacted]	06/28/2010-[redacted]	Amgen	評価
5.3.5.3-1 5.3.5.3-2	患者データ一覧表（Study 20101154）	[redacted]	—	Amgen	評価
5.3.5.3-1 5.3.5.3-2	患者データ一覧表（Study 20111155）	[redacted]	—	Amgen	評価
5.3.5.3-1 5.3.5.3-2	患者データ一覧表（Study 20090158）	[redacted]	—	Amgen	評価
5.3.5.3-1 5.3.5.3-2	患者データ一覧表（Study 20090159）	[redacted]	—	Amgen	評価
5.3.5.3-1 5.3.5.3-2	患者データ一覧表（Study 20110114）	[redacted]	—	Amgen	評価
5.3.5.3-1 5.3.5.3-2	患者データ一覧表（Study 20110115）	[redacted]	—	Amgen	評価
5.3.5.3-1 5.3.5.3-2	患者データ一覧表（Study 20110116）	[redacted]	—	Amgen	評価
5.3.5.3-1 5.3.5.3-2	患者データ一覧表（Study 20110117）	[redacted]	—	Amgen	評価
5.3.5.3-1 5.3.5.3-2	患者データ一覧表（Study 20110109）	[redacted]	—	Amgen	評価
5.3.5.3-1 5.3.5.3-2	患者データ一覧表（Study 20110231）	[redacted]	—	Amgen	評価
5.3.5.3-1 5.3.5.3-2	患者データ一覧表（Study 20120122）	[redacted]	—	Amgen	評価
5.3.5.3-1 5.3.5.3-2	患者データ一覧表（Study 20110110）	[redacted]	—	Amgen	評価
5.3.5.3-1 5.3.5.3-2	患者データ一覧表（Study 20120138）	[redacted]	—	Amgen	評価

5.3.5.3-1 5.3.5.3-2	患者データー覧表（Study 20120356）	[redacted]	－	Amgen	評価
5.3.5.3-1 5.3.5.3-2	患者データー覧表（Study 20120348）	[redacted]	－	Amgen	評価
5.3.5.3-1 5.3.5.3-2	患者データー覧表（Study 20110233）	[redacted]	－	Amgen	評価
5.3.5.3-1 5.3.5.3-2	患者データー覧表（Study 20110271）	[redacted]	－	Amgen	評価

第5部　臨床試験報告書
5.4　参考文献

資料番号	著者・表題・出典
5.4-1	Abbott RD, Donahue RP, Kannel WB, Wilson PW. The impact of diabetes on survival following myocardial infarction in men vs women: the Framingham Study. JAMA 1988;260:3456-60.
5.4-2	Abifadel M, Rabès JP, Devillers M, et al. Mutations and polymorphisms in the proprotein convertase subtilisin kexin 9 (PCSK9) gene in cholesterol metabolism and disease. Hum Mutat. 2009;30:520–529.
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添付すべき資料がない項目リスト
第3部　品質に関する文書
3.2.R　各極の要求資料

第4部　非臨床試験報告書
4.2.1.4　薬力学的薬物相互作用
4.2.2.3　分布
4.2.2.4　代謝
4.2.2.5　排泄
4.2.3.1　単回投与毒性試験
4.2.3.3　遺伝毒性試験
4.2.3.4.2　短期又は中期がん原性試験
4.2.3.4.3　その他の試験
4.2.3.5.2　胚・胎児発生に関する試験
4.2.3.5.4　新生児を用いた試験
4.2.3.7.1　抗原性試験
4.2.3.7.2　免疫毒性試験
4.2.3.7.3　毒性発現の機序に関する試験
4.2.3.7.4　依存性試験
4.2.3.7.5　代謝物の毒性試験
4.2.3.7.6　不純物の毒性試験

第5部　臨床試験報告書
5.3.1.1　バイオアベイラビリティ（BA）試験報告書
5.3.1.3　*In Vitro-In Vivo*の関連を検討した試験報告書
5.3.2　ヒト生体試料を用いた薬物動態関連の試験報告書
5.3.3.2　患者におけるPK及び初期忍容性試験報告書
5.3.3.4　外因性要因を検討したPK試験報告書
5.3.6　市販後の使用経験に関する報告書