SUPPLEMENTARY MATERIALS

Intravitreal Aflibercept for the Treatment of Diabetic Macular Edema in Routine Clinical Practice: Results from the 24-Month AURIGA Observational Study

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Supplementary Methods

Sample size

The sample size justification for the AURIGA diabetic macular edema (DME) treatment cohorts used a two-sided 95% confidence interval (CI) of ±1.72 letters to enable sufficient precision in the assessment of the mean change in visual acuity (VA) from baseline to Month 12 (primary endpoint) by country and by cohort. This calculation incorporated a conservative standard deviation (SD) estimate of 13 letters for the change in VA from baseline based on POLARIS, an observational study of ranibizumab in patients with DME [1, 2]. Assuming a drop-out rate of 20%, ≥275 patients each with treatment-naïve and pretreated DME needed to be enrolled in each of the participating countries to achieve sufficient precision for a by-country analysis (calculated using nQuery v.7.0; Statistical Solutions Ltd., Cork, Ireland). Based on the countries' level of interest in these cohorts, the AURIGA study aimed to enroll treatment-naïve patients from all countries/regions participating in the study (France, Germany, Italy, Mainland China, Middle East, Russia, and Taiwan; where the Middle East countries consisted of Egypt, Kuwait, Lebanon, Saudi Arabia, and the United Arab Emirates), and pretreated patients from Italy, Mainland China, and Russia. This resulted in an overall planned enrollment of 1925 and 825 patients with treatment-naïve and pretreated DME, respectively.

Exclusion criteria

Exclusion criteria included: any contraindications listed in the local intravitreal aflibercept (IVT-AFL) Summary of Product Characteristics (SmPC); concomitant therapy with a systemic anti-vascular endothelial growth factor (anti-VEGF) or pro-VEGF agent; concomitant therapy with any other agent for the treatment of DME in the study eye; structural damage to the center of the macula in either eye that is likely to preclude improvement in VA following the resolution of macular edema, or any other condition expected to permanently limit VA outcomes over the course of the study; patients with prior retinal surgery; laser photocoagulation (pan-retinal or macular) in the study eye within 90 days of Day 1; and a history of stroke or transient ischemic attacks within the last 6 months. In the pretreated cohort, only patients who had received prior treatment with steroids or intravitreal anti-VEGF agents other than IVT-AFL were eligible for enrollment. Additional exclusion criteria applied to pretreated patients were prior treatment with laser, anti-angiogenic drugs, ocular surgery, or intravitreal dexamethasone or triamcinolone within the last 3 months; a dexamethasone implant within the last 6 months; or a fluocinolone implant within the last 3 years.

COVID-19 sensitivity analysis

The date by which ≥100 confirmed Coronavirus Disease 2019 (COVID-19) cases were reported in a country was considered to be its COVID-19 start date. The COVID-19 start dates for each country reporting DME data were: China, January 22; France, February 29; Germany, March 1; Italy, February 23; Russia, March 13; and Taiwan, March 18 (all in 2020). In the 4 participating countries in the Middle East, the COVID-19 start date ranged from March 14 to March 18, and a start date of March 14 was applied to the pooled analysis of data from this region.

Supplementary Table 1 Reasons for switch to IVT-AFL treatment in the pretreated cohort

	Italy pretreated (n=75)	Russia pretreated (n=276)	Mainland China pretreated (n=33)	Overall DME pretreated (N=384)
Effort to extend treatment interval	0	2 (0.7)	2 (6.1)	4 (1.0)
Persistent intraretinal or subretinal fluid	38 (50.7)	209 (75.7)	1 (3.0)	248 (64.6)
Recurrence of fluid	32 (42.7)	40 (14.5)	3 (9.1)	75 (19.5)
New hemorrhage	0	1 (0.4)	3 (9.1)	4 (1.0)
Decreased vision	0	12 (4.3)	9 (27.3)	21 (5.5)
Lack of compliance	0	5 (1.8)	0	5 (1.3)
Patient request	2 (2.7)	7 (2.5)	9 (27.3)	18 (4.7)
Other	2 (2.7)	0	6 (18.2)	8 (2.1)
Missing	1 (1.3)	0	0	1 (0.3)

Values are n, %. DME, diabetic macular edema; IVT-AFL, intravitreal aflibercept.

Supplementary Table 2 Time (months) to treatment initiation per country

Treatment-naïve cohort	France (n=164)	Germany (n=150)	Italy (n=207)	Russia (n=280)	Middle East (n=203)	Taiwan (n=267)	Mainland China (n=207)	Overall cohort (N=1478)
Time from symptom occurrence to first IVT-AFL injection	7.9±15.0	5.2±19.5	25.2±58.8	17.3±24.3	13.4±39.3	9.7±28.8	6.6±10.5	12.7±32.8
Time from DME diagnosis to first IVT-AFL injection	5.9±13.6	4.4±19.4	21.9±57.0	10.1±17.6	8.7±35.1	7.6±25.1	2.4±6.9	9.0±29.8
Time from decision-to-treat to first IVT-AFL injection	0.4±0.7	0.5±0.5	0.8±0.9	0.5±1.3	0.6±1.6	0.7±1.2	0.1±0.2	0.5±1.1

Pretreated cohort	Italy (n=75)	Russia (n=276)	Mainland China (n=33)	Overall cohort (N=384)
Time from symptom occurrence to first IVT-AFL injection	44.6±57.0	29.3±23.5	22.1±32.1	31.6±33.8
Time from DME diagnosis to first IVT-AFL injection	40.0±55.8	21.9±19.8	15.3±25.4	24.8±31.5
Time from decision-to-treat to first IVT-AFL injection	0.7±0.7	1.2±2.3	0.1±0.1	1.0±2.0

Values are mean±SD. DME, diabetic macular edema; IVT-AFL, intravitreal aflibercept; SD, standard deviation.

Supplementary Table 3 Baseline visual acuity and central retinal thickness in each cohort, by country

	Treatment-naïve (n=1478)	Pretreated (n=384)
Baseline VA, letters		
France	67.1±10.6	
n	145	
Germany	65.0±15.3	
n	142	
Italy	54.5±21.0	58.3±18.9
n	200	73
Russia	54.2±19.2	48.7±19.4
n	280	275
Middle East	61.2±19.5	
n	191	
Taiwan	49.7±19.6	
n	258	
Mainland China	48.5±20.8	52.5±18.2
n	195	30
Total	**56.0±19.8**	**50.8±19.5**
N	**1411**	**378**
Baseline CRT, µm		
France	453±128	
n	149	
Germany	391±132	
n	116	
Italy	457±116	448±115
n	172	63
Russia	443±132	470±155
n	275	271
Middle East	403±131	
n	178	
Taiwan	433±120	
n	265	
Mainland China	474±216	454±143
n	137	26
Total	**437 ±140**	**465 ±148**
N	**1292**	**360**

Data are mean±SD unless otherwise stated. CRT, central retinal thickness; SD, standard deviation; VA, visual acuity.

Supplementary Table 4 Mean change in visual acuity (letters) from baseline to Month 12 stratified by gender

	Female treatment-naïve (n=723)	Male treatment-naïve (n=751)	Overall DME treatment-naïve (N=1478)[a]	Female pretreated (n=222)	Male pretreated (n=162)	Overall DME pretreated (N=384)
Baseline						
Mean VA	54.4±20.4	57.5±19.1	56.0±19.8	48.7±19.5	53.8±19.2	50.8±19.5
n, %	695 (96.1)	712 (94.8)	1411 (95.5)	221 (99.5)	157 (96.9)	378 (98.4)
Change from BL to Month 12						
Mean (95% CI)	6.0 (4.7, 7.3)	7.3 (6.0, 8.7)	6.7 (5.7, 7.6)	7.9 (5.5, 10.3)	6.8 (3.6, 10.0)	7.4 (5.5, 9.4)
n, %	632 (87.4)	637 (84.8)	1273 (86.1)	214 (96.4)	144 (88.9)	358 (93.2)

Data are from the FAS (LOCF) and values are mean±SD unless otherwise stated. The mean VA change data are based on the nearest VA assessment within the ±60-day visit window at Month 12.
[a]Four treatment-naïve patients had missing gender data in the Middle East cohort. BL, baseline; CI, confidence interval; DME, diabetic macular edema; FAS, full analysis set; LOCF, last observation carried forward; SD, standard deviation; VA, visual acuity.

Supplementary Table 5 Change in visual acuity (letters) from baseline to Months 6, 12, and 24 in each country and the overall treatment cohorts

	France	Germany	Italy	Russia	Middle East	Taiwan	Mainland China	Total
Treatment-naïve (n=1478)								
BL								
Mean VA	67.1±10.6	65.0±15.3	54.5±21.0	54.2±19.2	61.2±19.5	49.7±19.6	48.5±20.8	56.0±19.8
n	145	142	200	280	191	258	195	1411
Month 6								
Mean VA	72.8±12.3	69.8±14.0	61.2±20.8	62.3±17.3	66.9±14.9	59.2±17.7	57.0±19.1	63.5±17.7
n	149	145	157	270	154	252	159	1286
Change from BL	6.1±11.6	4.6±11.4	5.8±17.4	8.0±12.7	7.3±17.7	9.5±18.8	7.5±19.4	7.3±16.0
95% CI	4.1, 8.1	2.6, 6.5	3.1, 8.6	6.5, 9.5	4.4, 10.2	7.1, 11.8	4.4, 10.6	6.4, 8.2
n	133	137	153	270	145	244	152	1234
Month 12								
Mean VA	72.9±11.4	69.3±16.1	61.2±19.8	60.8±17.8	67.2±15.6	58.2±19.6	56.1±20.8	62.9±18.6
n	151	146	181	270	164	255	160	1327
Change from BL	5.9±10.7	4.0±11.4	6.3±19.3	6.5±13.6	8.0±18.9	8.4±20.9	6.4±21.7	6.7±17.4
95% CI	4.1, 7.8	2.1, 5.9	3.4, 9.1	4.9, 8.1	5.0, 11.0	5.8, 11.0	2.9, 9.9	5.7, 7.6
n	133	138	177	270	155	247	153	1273
Month 24								
Mean VA	72.6±11.0	70.3±16.1	60.0±20.8	58.9±18.5	65.8±17.4	57.6±20.4	56.0±20.7	62.1±19.2
n	152	146	182	270	170	256	160	1336
Change from BL	5.5±10.4	5.0±11.7	5.0±21.6	4.6±14.6	6.1±20.5	8.1±20.7	6.3±21.8	5.9±18.1
95% CI	3.7, 7.3	3.0, 6.9	1.8, 8.2	2.9, 6.4	2.9, 9.3	5.5, 10.7	2.8, 9.7	4.9, 6.9
n	134	138	178	270	160	248	153	1281
Pretreated (n=384)								
BL								
Mean VA			58.3±18.9	48.7±19.4			52.5±18.2	50.8±19.5
n			73	275			30	378
Month 6								
Mean VA			62.8±15.8	59.1±18.5			49.6±20.5	59.1±18.4
n			64	265			24	353
Change from BL			5.5±13.9	10.7±17.8			−6.1±22.3	8.7±17.9
95% CI			1.9, 9.0	8.5, 12.8			−16.0, 3.8	6.8, 10.6
n			62	264			22	348

Month 12						
Mean VA		61.1±18.6	57.6±20.0		52.0±19.9	57.9±19.8
n		70	268		25	363
Change from BL		3.8±14.8	9.1±19.0		−1.3±18.7	7.4±18.5
95% CI		0.2, 7.4	6.8, 11.4		−9.4, 6.7	5.5, 9.4
n		68	267		23	358
Month 24						
Mean VA		60.8±18.6	58.6±20.3		52.0±19.9	58.6±20.0
n		71	269		25	365
Change from BL		3.5±17.1	10.1±20.0		−1.3±18.7	8.1±19.7
95% CI		−0.6, 7.6	7.7, 12.5		−9.4, 6.7	6.1, 10.1
n		69	268		23	360

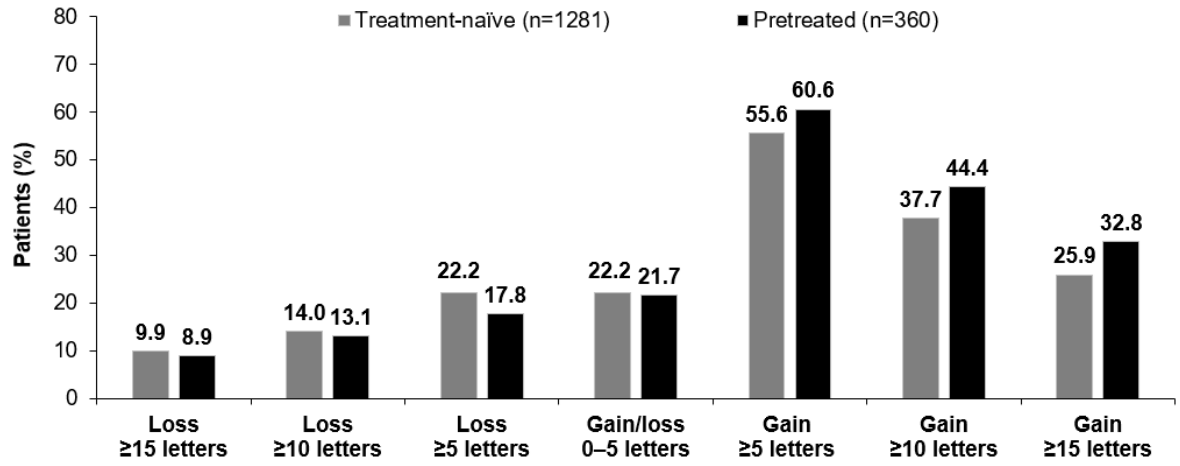
Data are mean ± SD unless otherwise stated. The mean VA change data are based on the nearest VA assessment within the ±30-day visit window at 6 months and within the ±60-day visit window at Months 12 and 24. BL, baseline; SD, standard deviation; VA, visual acuity.

Supplementary Table 6 Mean number of intravitreal aflibercept treatments for each country

	Treatment-naïve (n=1478)	Pretreated (n=384)
Until Month 6 visit		
France	5.0±1.4	
Germany	5.0±1.6	
Italy	4.1±1.4	4.3±1.2
Russia	4.4±1.5	4.1±1.5
Middle East	2.7±1.5	
Taiwan	4.0±1.5	
China	2.0±1.1	1.9±1.0
Total	3.8±1.7	3.9±1.5
Until Month 12 visit		
France	6.6±2.6	
Germany	7.1±3.2	
Italy	5.0±2.0	5.4±1.9
Russia	5.7±2.5	5.1±2.4
Middle East	3.4±2.2	
Taiwan	5.1±2.4	
China	2.1±1.2	2.1±1.2
Total	4.9±2.8	4.9±2.4
Until Month 24 visit		
France	7.8±4.0	
Germany	9.0±5.3	
Italy	5.6±2.7	6.2±2.8
Russia	7.0±3.9	6.6±3.7
Middle East	4.0±2.8	
Taiwan	5.6±2.9	
China	2.1±1.2	2.1±1.2
Total	5.7±3.9	6.2±3.6

Data are mean ± SD. SD, standard deviation.

Supplementary Figure 1 Letter gains and losses from baseline to Month 24 in treatment-naïve and pretreated patients with diabetic macular edema following intravitreal aflibercept treatment



References

1. Stefanickova J, Cunha-Vaz J, Ulbig M, Pearce I, Fernández-Vega Sanz A, Theodossiadis P, et al. A noninterventional study to monitor patients with diabetic macular oedema starting treatment with ranibizumab (POLARIS). Acta Ophthalmol. 2018;96(8):e942-e9.
2. Ulbig M, Höh H, Schmickler S, Wolf A, Dimopoulos S, Lorenz K, et al. [Treatment reality with ranibizumab in clinical routine use for patients with diabetic macular edema: 1-year results of the German POLARIS cohort]. Ophthalmologe. 2019;116(7):631-9.

Appendix I: AURIGA ethics approval committees

Name of Institutional Ethics Committee (IEC)/Institutional Review Board (IRB)	Approval number
SAUDI ARABIA	
King Faisal Specialist Hospital & Research Center - Jeddah IRB	RC-J/381/39
King Faisal Specialist Hospital & Research Center - Riyadh IRB	C380/541/39
King Khaled Eye Specialist Hospital IRB	RD/2600/6557-18
King Saud University Medical City IRB	18/0201/IRB
King Abdullah International Medical Research Center IRB (study site: King Fahd National Guard Hospital)	IRBC/1559/19
TAIWAN	
Taipei Veterans General Hospital IRB	2018-06-016CCU
Shin Kong Wu Ho-Su Memorial Hospital IRB	20180902C
Chi Mei Medical Center IRB	10711-004
National Taiwan University Hospital Research Ethics Committee	201808068RSC
Mackay Memorial Hospital IRB	18CT035be
Changhua Christian Hospital IRB	180817
China Medical University Hospital Research Ethics Committee	CMUH107-REC1-134
Kaohsiung Veterans General Hospital IRB	VGHKS18-CT10-06
Kaohsiung Medical University Hospital IRB	KMUHIRB-F(II)-20180137
National Cheng Kung University Hospital IRB	AB-CR-107-053
Tri-Service General Hospital IRB	2-108-01-015
Hualien Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation Research Ethics Committee	IRB109-050-B
Taipei Municipal Wan Fang Hospital IRB	N202003042
Far Eastern Memorial Hospital Research Ethics Review Committee	109077-F
CHINA	
Jinan Second People's Hospital IRB	Ji lun shen No. 2019-03
Weifang Eye Hospital IRB	Yuan Lun Kuai No.[2019]01
Shanghai General Hospital IRB	Yuan Lun Kuai No.[2019]43
Beijing Aier Intech Eye Hospital IRB	BJAIER2019IRB02
Medical Ethics Committee of the First Affiliated Hospital of Jinan University	[2019]Lun Shen Pi Ke No.030
Aier Eye Hospital IRB	GZAIER2019IRB11
Medical Ethics Committee of Tianjin Eye Hospital	Research Review No.201901
Medical Ethics Committee of Eye & Ent Hospital of Fudan University	[2019]Lun Shen Zi No.(2019049)

The Affiliated Eye Hospital of Shandong University of Traditional Chinese Medicine Medical Ethics Committee	SDTCMAEHEC2019-01
Medical Ethics Committee of Henan Eye Hospital	HNEECKY-2019(7)
The First Affiliated Hospital of Guangzhou University of Chinese Medicine Ethics Committee	No. ZYYEC2019-018-JT
Ethics Committee of Shenzhen Eyes Hospital	Shen Eye Lun Shen No. 20190701-01
Medical Ethics Committee of Tianjin Medical University Eye Hospital	2019KY-11
Medical Ethics Committee of Shandong Eye Institute	Qing Yan Lun Shen (Kuai) No.[2019]01
The First Affiliated Hospital of Zhengzhou University Scientific Research and Clinical Trial Ethics Committee	Drug-2019-079
Medical Ethics Committee of Joint Shantou International Eye Center of Shantou University and The Chinese University of Hong Kong	EC 20190911(4)-P04
Shanxi Eye Hospital Drug Clinical Trial IRB	SXEH2019IRB02
Xuzhou No.1 People's Hospital Medical Ethics Committee	xyyll[2019]22
IRB of Beijing Hospital	2019BJYYEC-107-01
Ethics Review Committee of Peking Union Medical College Hospital	B314
Ethics Committee of Xinhua Hospital Affiliated to Shanghai Jiaotong University School of Medicine	XHEC-C-2019-022-2
FRANCE	
All sites in France were approved by a central ethics committee: Comite de Protection des Personnes Ile de France III	Ref.CPP: 3551-NI
GERMANY	
Ethikkommission der Technischen Universität München	252/17S
Ärztekammer Nordrhein	2017386
Ethikkmmission der Otto-von Guericke-Universität an der Mediznischen Fakultät und am Univeritätsklinikum Magdeburg A.ö.R	174/17
Sächsische Landesärztekammer Ethikkommission	EK-BR-83/17-1
Ärztekammer Hamburg	MC-387/17
Ethikkommission an der Med. Fakultät der HHU Düsseldorf	Ihre Registrierungsnummer: 6250R
Ethikkommission an der Universitätsmedizin Greifswald	BB 049/18
Ethikkommission der Universität zu Lübeck	18-093
Ethikkommission an der Medizinischen Fakultät der Universität Leipzig	133/18-lk
Ethikkommission der Universitätsmedizin Göttingen	12/5/18
Ethikkommission der Landesärztekammer Rheinland Pfalz	2018 - 13331
Ethik-Kommission der Albert-Ludwigs-Universität Freiburg	308/18
Ethikkommission der Medizinischen Fakultät Heidelberg	S-224/2019
Ethik-Kommission des Fachbereichs Medizin der Johann Wolfgang Goethe-Universität	19-2019

Ethik-Kommission des FB Medizin, Gießen	178/18
Landesärztekammer Brandenburg	AS 43(bB)/2020
ITALY	
Comitato Etico Centrale IRCCS Lazio	Report 1 16-01-2018 - Study 62/17/FB
Comitato Etico Milano Area 3	108-032018
Comitato Etico Milano Area 3	107-032018
Comitato Etico dell'Insubria	136 of 2018
Comitato Etico Milano Area 3	247-052018
Comitato Etico Val Padana	34514 of 15/10/2018
Comitato Etico di Bergamo	125/18
Comitato Etico di Brescia	NP 3214
Comitato Etico Area Pavia	20180028515
Comitato Etico Milano Area 1	55895/2018
Comitato Etico Regionale Liguria	196/2018
Comitato Etico Regionale Liguria	196bis/2018
Comitato Etico Interaziendale AOU Maggiore della Carità, ASL BI, ASL NO, ASL BCL	438/CE
Comitato Etico Interaziendale	ASOOcul 18/01
Comitato Etico delle Sperimentazioni Cliniche della Provincia di Vicenza	91/18
Comitato Etico Campania Sud - ASL Napoli 3 Sud	85_r.p.s.o. Prot/SCCE 102716
Comitato Etico Università degli Studi della Campnia "Luigi Vanvitelli"	545 24/07/2018-Protocollo 13642/18
Comitato Etico Palermo 1	43282
Comitato Etico Catania 2	Prot 533/CE
Comitato Etico Catania 1	124/2018/PO
Comitato Etico Palermo 2	145 AG 2018
Comitato Etico Regionale delle Sperimentazioni Cliniche della Regione Toscana-Sezione area Vasta Centro	13410_oss
Comitato Etico Regionale delle Sperimentazioni Cliniche della Regione Toscana-Sezione area Vasta Nord Ovest	36768
Comitato Etico Regionale delle Sperimentazioni Cliniche della Regione Toscana-Sezione area Vasta Nord Ovest	39781
Comitato Etico Indipendente Azienda Ospedaliero-Universitaria "ConsorzialePoliclinico"	5615
Comitato Etico Indipendente Azienda Ospedaliero-Universitaria "Consorziale Policlinico"	5665
Comitato Etico Lazio 1	981/CE 1249
Comitato Etico dell'Università Sapienza	164 SA_2018-RIF CE 5079

Comitato Etico Lazio 2	69.18 A e B
Comitato Etico delle Aziende Sanitarie dell'Umbria	3293/18
Comitato Etico Calabria sezione Area Centro	08 of 18/01/2018
Comitato Etico Indipendente Azienda Ospedaliero-Universitaria di Cagliari	Prot PG/2018/11677
RUSSIA	
Independent Interdisciplinary Committee on Ethical Review of Clinical Trials	Extract from protocol №18 of the meeting of Independent Interdisciplinary Committee on Ethical Review of Clinical Trials dated Nov 10, 2017 (approval of the whole study)
Moscow City Independent Ethics Committee	Extract from protocol №15 of Moscow City Independent Ethics Committee ethical review dated Feb 21, 2018 (City Clinical Hospital №67 named after Vorokhobova L.A.)
Ethics Committee of State Novosibirsk Regional Clinical Hospital	Extract from protocol №2 of the meeting of Ethic Committee of State Novosibirsk Regional Clinical Hospital dated May 11, 2018 (State Novosibirsk Regional Clinical Hospital)
Independent Review Board of Kazan Regional Ophthalmological Hospital	Extract from protocol №2 of the meeting of Independent Review Board of Kazan Regional Ophthalmological Hospital dated Mar 11, 2019 (Kazan Regional Ophthalmological Hospital)
KUWAIT	
National MOH approval, Kuwait	1426
EGYPT	
National MOH approval, Cairo	IORG0005704/IRB0000687
LEBANON	
Hotel Dieu de France "BESH and Eye and Ear Hospital", Lebanon	No reference number
HLG/Dr. Raja Chaftari, Lebanon	2019-IRB-022
AUBMC/Abeer Dakik/Hamra, Lebanon	19157/BIO-2018-0196
UNITED ARAB EMIRATES	
MediClinic Airport/Khan Zakaullah/Dubai Production City, Public Pavillion, Dubai	MCME.CR.52.MAIR.2018
SKMC/Jaishen Rajah/Sheikh Khalifa Medical City, Abu Dhabi	REC-8.11.2018 [RS-551]
Moorfields Eye Hospital DHCC	REC/2019/P04
Dubai health authority "Medcare and Dubai Hospitals", Dubai	Medcare_DSREC-11/2018_07 /Dubai_DSREC-08/2020_34

Ministry of Health and Prevention "Al Qassimi Hospital", Dubai	MOHAP/DXB-REC-23/J.JA/2019
Tawam Hospital, Abu Dhabi	AA/SS/675
Maghrabi DHCC, Dubai	No reference number
Moorfields Abu Dhabi AUH, Abu Dhabi	REC/2019/P04

Appendix II: COMETA (Costs and OutcoMEs of ReTinAl Disease) questionnaire

1) How are you completing the questionnaire?
   a) By myself, no assistance required
   b) With assistance from family, partner, friend
   c) With assistance from health-care professional

2) What describes best your living environment?
   a) I am living alone
   b) I am living with family, spouse, partner, friend
   c) I am living in institutional care

3) What describes best your current activity?
   a) Full-time, self-employed
   b) Part-time
   c) Unemployed due to vision loss
   d) Unemployed
   e) Home maker
   f) Retired early due to vision loss
   g) Retired
   h) Employed, not further specified
   i) Other

4) In the past 3 months, did you have to take days of sick leave?
   a) No
   b) Yes
      Number of days of sick leave _____

5) In the past 3 months, did you have to reduce working hours permanently?
   a) No
   b) Yes
      Number of weekly working hours permanently reduced _____

6) In the past 3 months, did you have to change your type of work?
   a) No
   b) Yes

7) In the past 3 months, did you spend time in hospital because of vision impairment?
   a) No
   b) Yes
      Days spent in inpatient stay _____
      Days spent with a day visit or treatment _____
      Days spent at emergency unit _____
      Days spent in a specialized centre _____

8a) In the past 3 months, did you experience a fall/accident because of vision impairment?
   a) No
   b) Yes

8b) Did you receive treatment for your fall/accident?

a) No
b) Yes

8c) For your fall/accident, were you treated
a) At hospital
b) Ambulatory care

Days spent in inpatient stay _____
Days spent with a day visit or treatment _____
Days spent at Emergency unit _____
Days spent in a specialized centre _____

9) Number of visits to ophthalmologist / retinal specialist in the past 3 months _____
Duration:
a) Up to 1 hour
b) 2–3 hours
c) Half a day
d) More

10) Number of visits to general practitioner / family doctor in the past 3 months _____
Duration:
a) Up to 1 hour
b) 2–3 hours
c) Half a day
d) More

11) Number of visits to other medical specialist in the past 3 months _____
Duration:
a) Up to 1 hour
b) 2–3 hours
c) Half a day
d) More

12) Number of visits to orthoptist (vision specialist) in the past 3 months _____
Duration:
a) Up to 1 hour
b) 2–3 hours
c) Half a day
d) More

13) Number of visits to nurse in the past 3 months _____
Duration:
a) Up to 1 hour
b) 2–3 hours
c) Half a day
d) More

14) Number of visits to psychologist/counsellor in the past 3 months _____
Duration:
a) Up to 1 hour
b) 2–3 hours

c) Half a day
d) More

15) In the past 3 months, did you have to make changes to your living situation because of your vision loss?
a) No
b) Yes

16) Did you pay out of your own pocket?
a) No, fully reimbursed
b) Yes, but partly reimbursed
c) Yes

17) Number of days needing transportation in the past 3 months _____
Duration:
a) Up to 1 hour
b) 2–3 hours
c) Half a day
d) More

18) Number of days needing home help (household tasks) in the past 3 months _____
Duration:
a) Up to 1 hour
b) 2–3 hours
c) Half a day
d) More

19) Number of days needing social aid in the past 3 months _____
Duration:
a) Up to 1 hour
b) 2–3 hours
c) Half a day
d) More

20) Number of days needing nurse support in the past 3 months _____
Duration:
a) Up to 1 hour
b) 2–3 hours
c) Half a day
d) More

21) Number of days needing meals delivery in the past 3 months _____
Duration:
a) Up to 1 hour
b) 2–3 hours
c) Half a day
d) More

22) Number of days needing laundry service in the past 3 months _____
Duration:
a) Up to 1 hour
b) 2–3 hours

c) Half a day
d) More

23) Which aids have you used in the past 3 months because of poor vision?
a) Eye glasses
b) Stand/lamp magnifier
c) Speech synthesizer
d) Special diabetes device
e) TV glasses
f) Video magnifier
g) Computer within an integrated auditory system
h) Walking aids
i) Contact lenses
j) Telescopic lenses
k) Special phone
l) Enlarger screen
m) Hand-held magnifier
n) Medication dispenser

25a) Did you require assistance from your family or friends because of your vision problems in the past 3 months?
a) No
b) Yes

25b) Type of assistance needed
a) Basic self-care activities (hours per week_____)
b) Instrumental activities (hours per week_____)
c) Mobility help, transportation (hours per week_____)
d) Help with medication (hours per week_____)
e) Handling administrative tasks (hours per week_____)
f) Keeping company, spending time together (hours per week_____)

25c) Who was the caregiver who provided this assistance?
a) Spouse/partner
    - Not working
    - Working
b) Family member
    - Not working
    - Working
c) Friend/neighbour
    - Not working
    - Working

25d) Did your caregiver reduce/give up work?
a) No
b) Yes, reduced work hours
c) Yes, gave up work

Appendix III: AURIGA lead study investigators

Site ID	Study country	Lead study investigator
1915710002	Germany	Matthias Hartmann
1915710003	Germany	Erik Beeke
1915710004	Germany	Hendrik Fuchs
1915710005	Germany	Stephan Dunker
1915710006	Germany	Dirk Sander
1915710007	Germany	Tobias Duncker
1915710008	Germany	Hakan Kaymak
1915710010	Germany	Claudia Schuart
1915710011	Germany	Hüsnü Berk
1915710013	Germany	Bernd Kamppeter
1915710015	Germany	Ulrich Thelen
1915710016	Germany	Hans-Werner Görges
1915710017	Germany	Mirjam Gross
1915710018	Germany	Helmut Sachs
1915710019	Germany	Berthold Seitz
1915710020	Germany	Mohammad Osman Ramez
1915710021	Germany	Martin Scheffler
1915710022	Germany	Marianne Liedtke-Maier
1915710023	Germany	Peter Wiedemann
1915710023	Germany	Matus Rehak
1915710024	Germany	Matthias Grüb
1915710025	Germany	Andrea Michaela Wißmann
1915710026	Germany	Laszlo Kiraly
1915710027	Germany	Frank Röschinger
1915710028	Germany	Christian Karl Brinkmann
1915710030	Germany	Darius Schwarz
1915710030	Germany	Mohamed Khaireddine Ben Hafsa
1915710032	Germany	Thomas Kube
1915710033	Germany	Hita Dave
1915710035	Germany	Salvatore Grisanti
1915710042	Germany	Jakub Chmielowski
1915710043	Germany	Reka Seitz
1915710046	Germany	Fanni Molnar
1915710047	Germany	Simo Murovski
1915710048	Germany	Stefan Martin Heinrich
1915710050	Germany	Christian Ksinsik
1915710051	Germany	Rainer Guthoff
1915710055	Germany	Patrick Dillinger
1915710056	Germany	Katrin Lorenz
1915710058	Germany	Tim Hendrik Wirt
1915716001	France	Agnès Glacet-Bernard
1915716003	France	Céline Faure
1915716004	France	Christian Delhay
1915716005	France	Jérémie Halfon
1915716006	France	Camille Philippe-Zech

1915716007	France	Thi Ha Chau Tran
1915716009	France	Sébastien Guigou
1915716010	France	Mounir Benzerroug
1915716011	France	Jean-François Girmens
1915716012	France	Benjamin Wolff
1915716013	France	Christophe Baeteman
1915716014	France	Anne Robinet
1915716015	France	Minh-Huyen Nghiem-Buffet
1915716016	France	Rémi Servantie
1915716017	France	Frank Becquet
1915716018	France	Laurence Mahieu-Durringer
1915716019	France	Mate Streho
1915716023	France	Joël Uzzan
1915716024	France	Laurent Velasque
1915716025	France	Alban Comet
1915716026	France	Stéphanie Baillif
1915716028	France	Jean-Baptiste Conart
1915716029	France	Catherine Creuzot-Garcher
1915716030	France	Stéphane Delage
1915716031	France	Laurent Kodjikian
1915716033	France	Nicolas Leveziel
1915716034	France	Martine Mauget-Faÿsse
1915716035	France	Nicolas Nabholz
1915716036	France	Boris Rysanek
1915716037	France	Philippe Schauer
1915716038	France	Sarah Ayello-Scheer
1915716039	France	Eric SOUIED
1915716040	France	Ramin Tadayoni
1915716041	France	Hassiba Oubraham-Mebroukine
1915716042	France	Audrey Giocanti-Auregan
1915716043	France	Olivier Jankowski
1915716044	France	Édouard Koch
1915716045	France	Bernard Joannot
1915716046	France	Vincent Parier
1915716047	France	Jean-Claude Quintyn
1915716049	France	Adil Darugar
1915722001	Italy	Monica Varano
1915722002	Italy	Laura Sabato
1915722004	Italy	Simone Donati
1915722005	Italy	Stefano Gambaro
1915722006	Italy	Fabrizio Magnani
1915722007	Italy	Anna Paola Salvetti
1915722009	Italy	Luciano Quaranta
1915722012	Italy	Tommaso Rossi
1915722013	Italy	Massimo Nicolò
1915722014	Italy	Stela Vujosevic
1915722014	Italy	Stefano De Cillà
1915722015	Italy	Andrea Coggiola

1915722019	Italy	Simonetta Morselli
1915722021	Italy	Alfredo Greco
1915722022	Italy	Francesca Simonelli
1915722023	Italy	Maria Vadalà
1915722024	Italy	Clara Marino
1915722025	Italy	Andrea Russo
1915722026	Italy	Charles Anthony Martorana
1915722027	Italy	Gianni Virgili
1915722028	Italy	Franco Passani
1915722030	Italy	Marco Nardi
1915722031	Italy	Claudio Furino
1915722035	Italy	Gianluca Scuderi
1915722037	Italy	Mauro Schiavone
1915722038	Italy	Carlo Cagini
1915722039	Italy	Giovanna Carnovale Scalzo
1915751001	Russia	Sergey Grigorov
1915751002	Russia	Ekaterina Zakharova
1915751004	Russia	Zuleikha Abdulgazizova
1915751005	Russia	Elena Krivolapova
1915751006	Russia	Elina Santoro
1915751007	Russia	Sergey Obikhod
1915751008	Russia	Natalia Balalaeva
1915751009	Russia	Irina Kovelenova
1915751010	Russia	Olga Dobroradnykh
1915751011	Russia	Andrey Yavorskiy
1915751012	Russia	Andrey Goydin
1915751013	Russia	Liya Ramazanova
1915751013	Russia	Krisitina Protasova
1915751014	Russia	Evgeny Chernov
1915751015	Russia	Tatyana Kamenskih
1915751016	Russia	Anzhella Fursova
1915751017	Russia	Oleg Kolenko
1915751018	Russia	Yana Martusevich
1915751019	Russia	Alexander Doga
1915751020	Russia	Alla Ryabtseva
1915751021	Russia	Aliya Yarmukhametova
1915751022	Russia	God'ko Nadezhda
1915751023	Russia	Nikolay Logunov
1915751024	Russia	Rosa Tokinova
1915751025	Russia	Tatiana Sokolova
1915751026	Russia	Svetlana Kim
1915751027	Russia	Kseniya Dashenko
1915751028	Russia	Aleksandr Kolesnikov
1915751029	Russia	Tatiana Yurieva
1915751030	Russia	Anastasia Shaidt
1915751031	Russia	Elena Zhukova
1915751032	Russia	Olga Parfentseva
1915754001	China	Fangju Han

1915754002	China	Xianyong Sun
1915754003	China	Xun Xu
1915754004	China	Wei Gu
1915754005	China	Jingxiang Zhong
1915754006	China	Hongjie Ma
1915754007	China	Mei Han
1915754008	China	Qing Chang
1915754009	China	Xingrong Wang
1915754010	China	Zhaoxia Zhao
1915754010	China	Ke Fan
1915754011	China	Xiaoyi Yu
1915754012	China	Guoming Zhang
1915754013	China	Xiaorong Li
1915754014	China	Haifeng Xu
1915754015	China	Qiuming Li
1915754016	China	Haoyu Chen
1915754017	China	Bin Sun
1915754018	China	Suyan Li
1915754019	China	Hong Dai
1915754020	China	Youxin Chen
1915754021	China	Peiquan Zhao
1915761001	Taiwan	Shih-Jen Chen
1915761002	Taiwan	Cheng-Kuo Cheng
1915761003	Taiwan	Shu-Chun Kuo
1915761005	Taiwan	Hsiang-Ling Tsai
1915761006	Taiwan	Jian-Sheng Wu
1915761007	Taiwan	Wen-Lu Chen
1915761008	Taiwan	Shwu-Jiuan Sheu
1915761009	Taiwan	Wen-Chuan Wu
1915761010	Taiwan	Sheng-Min Hsu
1915761011	Taiwan	Jiann-Torng Chen
1915761012	Taiwan	Ming-Shan He
1915761013	Taiwan	Chien-Liang Wu
1915761014	Taiwan	Jia-Kang Wang
1915784001	Egypt	Noha Khater
1915784002	Egypt	Omar Barrada
1915784003	Egypt	Ahmed El-Sawy Habib
1915784007	Egypt	Maged Mikhael
1915784008	Egypt	Amr Bessa
1915784011	Egypt	Magdy Moussa
1915787001	Saudi Arabia	Marco Mura
1915787002	Saudi Arabia	Marwan Abouammoh
1915787003	Saudi Arabia	Selwa Al-Hazzaa
1915787004	Saudi Arabia	Saad Waheeb
1915787005	Saudi Arabia	Mohammad Hazzazi
1915795501	Lebanon	Riad Bijanny
1915795503	Lebanon	Alexander Jalkh
1915795901	United Arab Emirates	Usman Mahmood

1915795902	United Arab Emirates	Ahmed ElBarky
1915795903	United Arab Emirates	Avinash Gurbaxani
1915795904	United Arab Emirates	Prasan Rao
1915795905	United Arab Emirates	Patricio Lorenzo
1915795906	United Arab Emirates	Fatima Al-Amiri
1915795907	United Arab Emirates	Alaa Attawan
1915795908	United Arab Emirates	Amr Farid
1915795909	United Arab Emirates	Madhava Rao
1915795910	United Arab Emirates	Firdaus Sukhi
1915795912	United Arab Emirates	Igor Kozak