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Dexamethasone intravitreal implant in treatment-naïve diabetic macular oedema: findings from the prospective, multicentre, AUSSIEDEX study

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ABSTRACT

Aim To evaluate the effectiveness of dexamethasone intravitreal implant 0.7 mg (DEX; Ozurdex) monotherapy in the patient subgroup of the AUSSIEDEX study with treatment-naïve diabetic macular oedema (DME).

Methods The open-label, prospective, phase 4, real-world study included pseudophakic eyes and phakic eyes scheduled for cataract surgery that were treatment-naïve or non-responsive to antivascular endothelial growth factors. No eyes were excluded based on baseline best-corrected visual acuity (BCVA) or central subfield retinal thickness (CRT). After the initial DEX injection at the baseline visit, reinjection was permitted at ≥16-week intervals. Week-16 and week-52 visits were mandatory. Primary endpoints were changes in mean BCVA and CRT from baseline to 52 weeks.

Results Of 200 eyes enrolled in the AUSSIEDEX study, 57 were treatment-naïve. Baseline mean BCVA was 58.8 letters and baseline mean CRT was 418.6 µm; changes in mean BCVA and CRT from baseline to 52 weeks in this subgroup were 3.4 letters (p=0.042) and −89.6 µm (p<0.001), respectively, with a mean 2.5 injections. The change in mean CRT from baseline was −55.8 µm at week 16 (p<0.001). The most common adverse event was increased intraocular pressure (IOP), with 20.0% of eyes requiring IOP-lowering medication. One patient was discontinued due to increased IOP. No eyes required filtration surgery. No serious, treatment-related ocular adverse events were reported.

Conclusion In this largest prospective, real-world study of DEX monotherapy for DME to date, DEX significantly improved CRT and BCVA at 52 weeks in treatment-naïve eyes, without new safety concerns, supporting DEX use in treatment-naïve DME.

Trial registration number NCT02731911.

INTRODUCTION

The International Diabetes Federation estimated that 6.5% (n=1 133 000/17 519 000) of the Australian adult population had diabetes in 2017,[1] and projections of ≥2 million for 2025 and 3.5 million for 2033 indicate that this proportion will keep increasing.[2] Consistent with these data, in 2019, approximately 463 million adults worldwide aged 20–79 years were diagnosed with diabetes, and the number is expected to rise to 700 million by 2045.[3] This increase of ≥48% is concerning because diabetes can cause loss of central vision through progressive diabetic macular oedema (DME).[4 5] DME has become a main cause of vision loss among individuals of working age and the European Society of Retina Specialists described diabetes-related retinal disease as the plague of the coming decades.[5]

Intravitreal antivascular endothelial growth factor (anti-VEGF) therapy currently represents the standard of care in the management of sight-threatening DME.[4] In pivotal clinical studies, bevacizumab (Avastin, Genentech, San Francisco, California, USA),[6–9] ranibizumab (Lucentis, Genentech)[10–12] and aflibercept (Eylea, Regeneron Pharmaceuticals, Tarrytown, New York, USA)[13 14] effectively improved both visual and anatomic outcomes in DME. The treatment burden associated with anti-VEGF agents can be high as frequent injections[15 16] and monitoring/follow-up visits[17–20] are often needed, and not all eyes respond optimally to anti-VEGF therapy.[21] Intravitreal corticosteroids provide broader anti-inflammatory effects, inhibiting synthesis of VEGFs and other proinflammatory mediators leading to DME.[22] Compared with triamcinolone acetonide and fluocinolone acetonide intravitreal corticosteroids used to treat DME, dexamethasone was also shown to be less lipophilic and exhibit less partitioning in the trabecular meshwork and lens,[23] which could potentially reduce side effects. The intravitreal dexamethasone implant (DEX; Ozurdex 0.7 mg, Allergan, an AbbVie company, North Chicago, Illinois, USA) was developed as an alternative to anti-VEGF therapies to reduce treatment burden and the risks associated with injections.[24] In a pooled analysis of randomised, multicentre, masked, sham-controlled, phase 3 studies identically designed to assess the safety and efficacy of DEX in DME previously treated with anti-VEGF agents or laser, a mean 4.1 injections over 3 years produced statistically significant improvements in visual and anatomic outcomes from baseline, compared with sham treatment, with a similar incidence of adverse events adjusted for treatment exposure time.[25]

In June 2015, DEX was approved in Australia for the treatment of DME (with reimbursement for pseudophakic eyes and phakic eyes scheduled for cataract surgery) based on results from the phase 3 studies. The AUSSIEDEX study, currently the largest prospective study of DME monotherapy in the real-world setting, was designed to evaluate visual, anatomic and safety outcomes of DEX monotherapy in DME. This manuscript summarises key outcomes in the overall population, while

focusing on findings in the treatment-naïve subgroup of enrolled patients, for whom there is increasing interest in using DEX as first-line therapy.

METHODS

AUSSIEDEX study design

This prospective, observational, multicentre, open-label, non-randomised, phase 4 study was conducted in accordance with the International Council for Harmonisation Good Clinical Practice guidelines, the Council for International Organizations of Medical Sciences International Ethical Guidelines, the Declaration of Helsinki, and all applicable local laws/regulations. All patients provided written informed consent before initiating treatment.

AUSSIEDEX study population

Eligible patients were ≥18 years of age and had vision-threatening, treatment-naïve or previously treated DME in pseudophakic eyes or phakic eyes scheduled for cataract surgery. The physician must have decided to treat with DEX before the patient could be screened for study participation.

The key ophthalmic exclusion criteria were previous DEX treatment, use of concurrent intravitreal injections, and contraindications to DEX per product information.[26] There were no eligibility restrictions in terms of best-corrected visual acuity (BCVA) or central subfield retinal thickness (CRT) at baseline. For patients receiving bilateral treatment, the first eye treated was included in the study.[26]

Enrolled patients were stratified by prior therapy. Eyes could be treatment-naïve, with laser photocoagulation being allowed, or non-responsive to anti-VEGF therapy, defined as failure to achieve a ≥5-letter gain in BCVA and/or clinically significant CRT improvement after 3–6 anti-VEGF injections.

Treatments and assessments

DEX was administered intravitreally per product information.[26] Following the initial injection at the baseline visit, retreatment was permitted at ≥16-week intervals until week 52, per physician's judgement.[26] Treatment with laser photocoagulation was allowed, at the physician's discretion, starting ≥16 weeks after the first DEX injection. All patients who received laser treatment for DME could receive additional DEX treatments and were to remain in the study for evaluation at week 52.

Baseline measurements were taken on the day of the first DEX injection. Protocol-defined, mandatory follow-up visits were scheduled at 16±4 and 52±4 weeks; other follow-up visits were at the physician's discretion. BCVA assessments using logMAR charts and spectral domain optical coherence tomography, if performed, were collected at each visit, or up to 3 days before a scheduled injection. The nature and frequency of adverse events, frequency of DME-related laser treatment, intraocular pressure (IOP), use of IOP-lowering medications, and biomicroscopic and ophthalmoscopic findings were assessed at all visits. Ocular surgeries, including vitrectomy as well as cataract or glaucoma surgeries, and glaucoma-related laser treatment required after the first DEX injection were also recorded.

Outcomes and analyses

The mean number of DEX injections at week 52 was reported. The primary effectiveness endpoints were the changes in mean BCVA and CRT from baseline to week 52. Secondary effectiveness endpoints included: changes in mean BCVA and CRT from baseline at weeks 6, 16 and 24; proportion of patients with a ≥15-letter, ≥10-letter and ≥5-letter gain, no change, or ≥15-letter, ≥10-letter and ≥5-letter loss at weeks 6, 16, 24 and 52; proportion of patients with central foveal threatening lipid deposition at weeks 6, 16, 24 and 52; and change in mean BCVA from baseline at weeks 6, 16, 24 and 52, stratified by BCVA level at baseline, that is, ≥70 letters, driving vision standard, and ≤34 letters, legal blindness. A post hoc analysis of the mean BCVA and mean change in BCVA from baseline at each visit by number of DEX injections received during the study period was also performed.

The effectiveness population included all patients who received ≥1 DEX injections in the study eye and attended ≥1 postbaseline visit, mandatory or other, in addition to the baseline visit. If multiple visits occurred around weeks 6, 16, 24 and 52, the observations closest to the target day were analysed.

In this manuscript, the primary effectiveness endpoints are presented for the overall population and subgroup of treatment-naïve patients, as well as the subgroup of treatment-naïve patients who were also pseudophakic at baseline. Secondary effectiveness endpoints were analysed in treatment-naïve patients.

Safety endpoints included: the incidence of adverse events and adverse events of special interest, identified as important DEX-related adverse events or potential risks during the registration clinical trials; IOP at each visit; proportion of patients with IOP change ≥10, ≥25 or ≥35 mm Hg from baseline at any time; and proportion of patients requiring IOP-lowering medications and/or glaucoma-related laser or incisional surgical treatment during the study.

Statistical analyses were performed with SAS software V.9.2 or higher (SAS Institute, Cary, North Carolina, USA), without imputation for missing values unless otherwise indicated. Continuous variables were summarised by mean and SD; categorical variables were summarised by frequency and percentage. Statistical analyses of effectiveness endpoints were based on Student's paired t test, with p values for continuous variables, or the Clopper-Pearson method, with 95% CI for categorical variables. All p values are two sided, unless indicated otherwise, and $p<0.05$ indicated statistical significance.

RESULTS

Patient disposition, demographics and baseline characteristics

The AUSSIEDEX study was conducted between 29 April 2016 and 22 October 2018 in 25 ophthalmology clinics in Australia. Of 200 patients enrolled, 57 (28.5%) were treatment-naïve and 41/57 (71.9%) completed the study (online supplemental figure 1). The treatment-naïve effectiveness and safety populations included 55 (96.5%) patients, as 2 enrolled patients did not receive any DEX treatment. Of these 55 patients, 40 (72.7%) were pseudophakic at baseline, and 5 (9.1%) patients underwent cataract surgery during the study. Although no formal statistical comparisons were performed, treatment-naïve patient demographics and baseline characteristics appeared to be comparable to those of the overall safety population (n=196; table 1).

Key outcomes in the overall population

The mean number of DEX injections was 2.4 (95% CI 2.2 to 2.5), ranging from 1 to 4 (median, 2.5); 49 (25.0%) patients received 1 injection, 49 (25.0%) received 2 injections, 75 (38.3%) received 3 injections and 23 (11.7%) received 4 injections.

The change in mean BCVA from baseline was statistically significant at weeks 6, 16 and 24 (≥2.2 letters, p≤0.023; figure 1A), whereas the change in mean CRT from baseline

Table 1 Patient demographics and baseline characteristics

Safety population	Total (N=196)*	Treatment-naïve subgroup (N=55)
Mean age (SD), years	67.5 (9.3)	69.5 (10.3)
<65, n (%)	69 (35.2)	14 (25.5)
≥65, n (%)	127 (64.8)	41 (74.5)
Sex, n (%)		
Male	121 (61.7)	33 (60.0)
Female	75 (38.3)	22 (40.0)
Race, n (%)		
Caucasian	156 (79.6)	42 (76.4)
Asian	15 (7.7)	3 (5.5)
Middle Eastern	6 (3.1)	3 (5.5)
Pacific Islander	3 (1.5)	1 (1.8)
Aboriginal	4 (2.0)	0
African	2 (1.0)	0
Maori	1 (0.5)	0
Other	9 (4.6)	6 (10.9)
Mean DME duration (SD), years	3.7 (3.6)	2.9 (4.6)
Lens status, n (%)		
Pseudophakic	142 (72.4)	40 (72.7)
Phakic	54 (27.6)	15 (27.3)
Study eye, n (%)		
Right	98 (50.0)	24 (43.6)
Left	98 (50.0)	31 (56.4)
Mean IOP (SD), mm Hg	14.6 (3.7)	14.0 (3.7)
History of glaucoma, n (%)		
Yes	14 (7.1)	7 (12.7)
No	182 (92.9)	48 (87.3)
Mean BCVA (SD), letters†	57.3 (19.0)	55.8 (18.7)
Range	2, 96	10, 88
Mean CRT (SD), µm†	418.0 (119.4)	418.6 (106.3)
Range	76, 965	248, 702
Central foveal-threatening lipid deposition, n (%)‡	72 (36.7)	21 (38.2)

*Included the treatment-naïve and non-responder subgroups.
†Efficacy population.
‡Based on the presence of hard exudates and central foveal involvement.
BCVA, best-corrected visual acuity; CRT, central retinal thickness; DME, diabetic macular oedema; IOP, intraocular pressure.

was statistically significant at all visits (≥−39.4 µm, p<0.001; figure 1B). In an effort to determine whether the number of DEX injections received during the study period might have impacted the visual outcomes, mean BCVA and the mean change in BCVA from baseline were assessed at each visit in patients who received a total of 1, 2, 3 or 4 DEX injections. Although formal statistical analyses were not performed, a notable positive change in BCVA from baseline at week 52 (n=14) was observed in patients who received only one injection, which could suggest more stable disease in those patients (online supplemental table 1).

In total, 108 (55.1%) patients reported ≥1 treatment-emergent adverse event(s). Increase in IOP was the most common treatment-emergent adverse event and adverse event of special interest, reported in 38 (19.4%) patients (table 2) and associated with 2 (1.0%) discontinuations. Increase in IOP from baseline ≥10 mm Hg was only reported after the third injection (n=1) and at study end (n=2); all increases in IOP were <25 mm Hg from baseline. At week 52 (n=144), 28 (19.4%) patients required IOP-lowering medication, compared with 39/192 (20.3%) at baseline. There was one serious drug-related adverse event (IOP increase), but none of the enrolled eyes required glaucoma-related laser or incisional surgical treatment during the study.

Treatment, effectiveness and safety in treatment-naïve patients

In this subgroup (N=55), 41 patients had 12 months of follow-up (online supplemental figure 1) and the mean number of DEX injections received over 52 weeks was 2.5 (95% CI 2.2 to 2.7), ranging from 1 to 4 (median, 3.0); 13 (23.6%) patients received 1 injection, 12 (21.8%) received 2 injections, 22 (40.0%) received 3 injections and 8 (14.5%) received 4 injections. The mean (SD) injection interval was 135.7 (38.8) days. One patient required laser photocoagulation for DME in the study eye.

The changes in mean BCVA and CRT from baseline to week 52, primary endpoint, were 3.4 letters and −89.6 µm, respectively, and statistically significant (figure 1C,D). In addition, the change in mean BCVA from baseline was statistically significant at week 6 (2.8 letters; figure 1C), whereas the change in mean CRT from baseline was statistically significant at weeks 6, 16 and 24 (≥−55.8 µm; figure 1D).

Over 78% of treatment-naïve patients with available data reported a gain or no change in BCVA from baseline at weeks 6, 16, 24 and 52 (figure 2); at week 52, 42.5% gained ≥5 letters, including 15.0% who gained ≥15 letters, 40.0% reported no change in BCVA, that is, gain or loss of 4 letters or less, and 17.5% lost ≥5 letters, including 5.0% who lost ≥15 letters.

The number of treatment-naïve patients did not allow statistically meaningful stratification of the changes in mean BCVA from baseline by baseline BCVA (online supplemental table 2). In treatment-naïve patients who were pseudophakic at baseline (n=39), the changes in mean BCVA from baseline were statistically significant at weeks 6 (3.6 letters) and 16 (3.2 letters; p≤0.044), whereas the mean (SD) changes in CRT from baseline were statistically significant at all time points (≥−54.2 µm; p≤0.001; online supplemental table 3). The proportion of patients with central foveal threatening lipid deposition was 25.5% (n=14/55), 21.8% (n=12/55), 12.7% (n=7/55) and 18.2% (n=10/55) at weeks 6, 16, 24 and 52, respectively, compared with 38.2% (n=21/55) at baseline.

Consistent with findings in the overall AUSSIEDEX population, IOP increase was the most common treatment-emergent adverse event and adverse event of special interest, reported in 11 (20.0%) patients (table 2) and leading to 1 discontinuation (online supplemental figure 1).

Mean IOP remained under 18.0 mm Hg at all visits, compared with 14.0 mm Hg at baseline (table 3). The changes in mean IOP from baseline were ≤3.9 mm Hg at each visit. At week 52, 15.0% (n=6/40) of patients exhibited IOP ≥21 mm Hg, compared with 3.7% (n=2/54) at baseline (table 3). The proportion of patients with IOP increases ≥10 mm Hg was ≤13.0% at weeks 16, 24 and 52, and there were no reports of IOP increase ≥25 mm Hg (table 3). Among treatment-naïve patients with available data at week 52 (n=40), 8 (20.0%) required IOP-lowering medication for IOP increase, compared with 12/54 (22.2%) at baseline, after the first injection (table 3). There were no serious drug-related (ocular or not) adverse events in this subgroup of patients.

DISCUSSION

To date, the AUSSIEDEX study is the largest prospective, real-world study evaluating the effectiveness of DEX as DME monotherapy in treatment-naïve patients and anti-VEGF non-responders. In the treatment-naïve cohort, a mean of 2.5 DEX

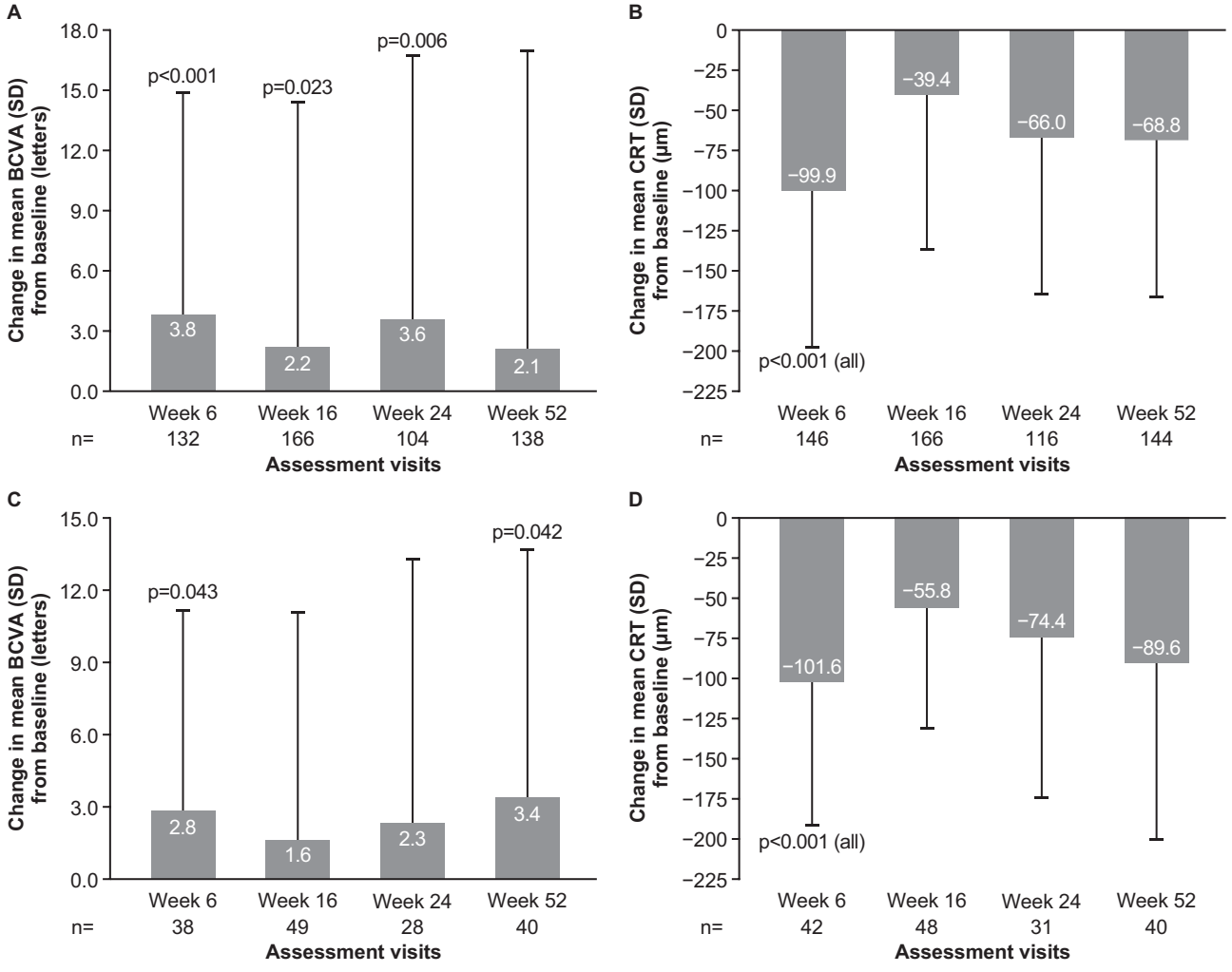

Figure 1 Change in mean (SD) (A, C) BCVA and (B, D) CRT from baseline over time in the overall population (A, B) and treatment-naïve patients (C, D). BCVA, best-corrected visual acuity; CRT, central retinal thickness.

administrations over 52 weeks yielded statistically significant improvements in BCVA from baseline at weeks 6 and 52, and in CRT at all postbaseline visits. In comparison, a mean of 2.4 DEX administrations over 52 weeks in the overall population resulted in similar CRT observations, and statistically significant improvements in BCVA from baseline at weeks 6, 16 and 24. The smallest changes in mean BCVA and CRT were observed at 16 weeks, possibly because all patients had received only 1 DEX injection and were eligible for a second DEX injection at that visit. After the first 16 weeks, the treatment schedule became more individualised as each patient's needs determined whether retreatment was appropriate or not, potentially preventing observation of another trough effect.

Table 2 Treatment-emergent adverse events reported in ≥2% of patients in the overall safety population or treatment-naïve subgroup

Treatment-emergent adverse events, n (%)	Overall population (N=196)	Treatment-naïve subgroup (N=55)
Total	108 (55.1)	45 (81.8)
Treatment related	45 (23.0)	14 (25.5)
Serious*	1 (0.5)	0
Increase in intraocular pressure†	38 (19.4)	11 (20.0)
Conjunctival haemorrhage	8 (4.1)	2 (3.6)
Vitreous haemorrhage	5 (2.6)	1 (1.8)
Influenza	5 (2.6)	1 (1.8)
Fall	5 (2.6)	1 (1.8)
Eye irritation	4 (2.0)	1 (1.8)
Macular hole	2 (1.0)	2 (3.6)
Diabetic ulcer	2 (1.0)	2 (3.6)

*Increase in intraocular pressure from baseline.
†Compared with baseline.

The AUSSIEDEX study population differed from those of the phase 3 clinical trials of DEX (MEAD[25]), ranibizumab (RISE/RIDE[11 12]) and aflibercept (VIVID/VISTA[13 14]). In our study, there were less stringent inclusion and exclusion criteria. There were no baseline visual acuity restrictions, whereas MEAD, RISE/RIDE and VIVID/VISTA required that visual acuity be between 20/50 (65 letters) and 20/200 (35 letters),[25] 20/40 (70 letters) and 20/320 (25 letters),[11] and 20/40 (70 letters) and 20/320 (25 letters),[13] respectively. Although mean BCVA at baseline appeared similar across those studies, varying from 54.7 to 60.8 letters, the BCVA range at baseline was considerably broader in the AUSSIEDEX study (10–88 letters in the treatment-naïve subgroup) than in the clinical trials. These differences could have introduced floor/ceiling effects,[27] limiting the effect of DEX on the anatomic and functional outcomes evaluated in this analysis. In comparison, the change in mean BCVA from baseline at 12

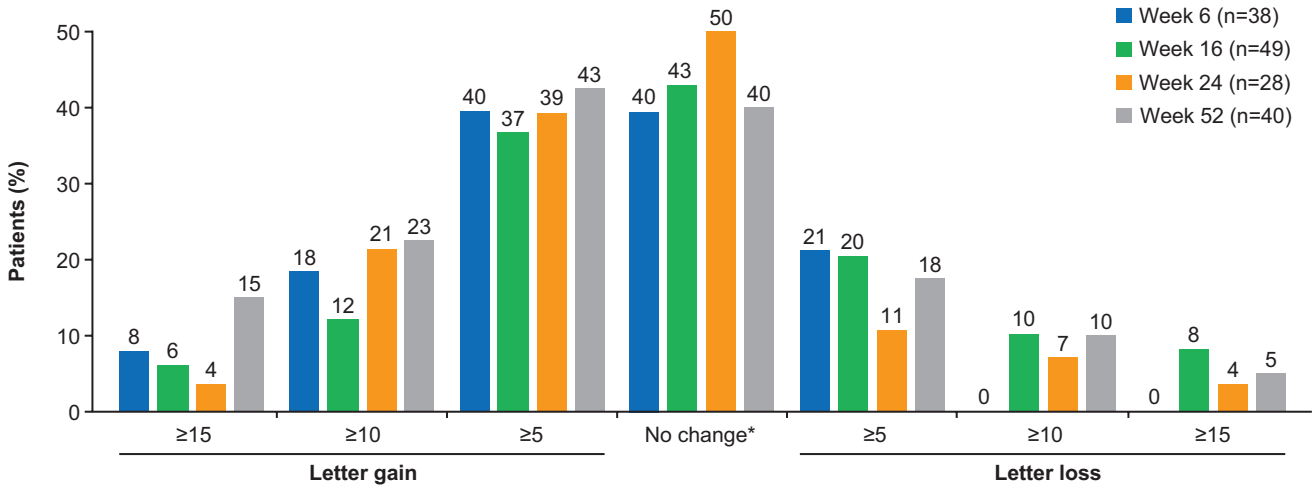

Figure 2 Proportion of treatment-naïve patients with a ≥15-letter, ≥10-letter and ≥5-letter gain, no change, or ≥15-letter, ≥10-letter and ≥5-letter loss from baseline at each visit. *No change means a gain or loss of 4 letters or less.

months was statistically significant in MEAD (~2.5 letters),[25] RISE/RIDE (≥10 letters)[11] and VIVID/VISTA (≥10.7 letters).[13] The longer duration of DME in the present study (2.9 years in the treatment-naïve subgroup), compared with 2.0[25] and ≤2.1[11] years (details not provided in VIVID/VISTA[13]), could also explain the reduced effects of DEX reported herein, further suggesting that earlier referral for treatment might improve outcomes. The mean age was also higher in the AUSSIEDEX study, 67.5 years in the overall population and 69.5 years in the treatment-naïve subgroup, than in the aforementioned phase 3 studies, in which mean age was 61.7–64.2 years.[11 13 25] In addition, patients had less macular fluid at baseline and mean CRT was thinner in the AUSSIEDEX study, 418.0 µm in the overall population and 418.6 µm in the treatment-naïve subgroup, than in the phase 3 clinical trials, in which mean CRT was 447.4–540.0 µm.[11 13 25]

Notably, our findings are consistent with those of a recently published systematic review of real-world studies (n=21) of DEX monotherapy in DME management, which indicated that the average number of injections administered per 6 months was 1.3, or approximately 2.6 per year, compared with 2.4 (overall AUSSIEDEX population) and 2.5 (treatment-naïve patients) in this analysis, and that DEX was well tolerated overall.[28] One of the studies included in the systematic review involved 14 consecutively enrolled patients/eyes with DME, treatment-naïve and previously treated, in whom anti-VEGF therapy was contraindicated. A mean of 1.71 DEX injections in 1 year produced statistically significant improvements in BCVA and CRT from baseline (means, 0.25 logMAR and 484 µm) at 12 months, +0.15 logMAR (or ~7.5 letters) and −173 µm, respectively (p<0.001 for both),[29] in line with our data. In another study included in the systematic review, statistically significant improvements in BCVA (+5.2 letters; p<0.001) and CRT (−181 µm; p<0.001) from baseline (means, 52.0 letters and 537.6 µm, respectively) were observed at 12 months in 54 patients/eyes who received a mean of 2.1 DEX injections.[30] In contrast, a study of 84 patients (113 eyes) included in the systematic review concluded that with a mean of 1.44 DEX injections, the changes in BCVA and CRT from baseline (means, 43.5 letters and 462.8 µm) were not statistically significant at 12 months, that is, +4.2 letters and −49.6 µm, respectively (p>0.05 for both).[31] Whether the difference in outcomes in the latter study is due to the lower mean number of injections, population-specific factors and/or other reasons is unknown and should be investigated in future studies. This is especially important when considering that in a prospective case series of 153 phakic patients with treatment-naïve DME, published after the systematic review and in which baseline corrected distance visual acuity (CDVA) and CRT were 20/40–20/200 and >300 µm, respectively, a mean (SD) 1.6 (0.8)

Table 3 Mean IOP and related variables at each visit

Treatment-naïve subgroup (N=55)					
Visits	Mean (SD) IOP, mm Hg	IOP ≥21 mm Hg, n (%)	IOP increase ≥10 mm Hg, n (%)	IOP increase ≥25 mm Hg, n (%)	Patients who required 1/2/≥3 IOP-lowering medications, n (%)
Baseline	14.0 (3.7)	2 (3.7)	0	0	5 (9.3)/1 (1.9)/6 (11.1)
N	54	54	54	54	54
Week 6	17.9 (7.7)	11 (23.9)	6 (13.0)	0	3 (6.5)/1 (2.2)/6 (13.0)
N	46	46	46	46	46
Week 16	14.8 (3.7)	4 (8.2)	1 (2.0)	0	4 (8.2)/1 (2.0)/5 (10.2)
N	49	49	49	49	49
Week 24	16.0 (6.3)	4 (12.5)	3 (9.4)	0	3 (9.4)/1 (3.1)/3 (9.4)
N	32	32	32	32	32
Week 52	16.0 (4.9)	6 (15.0)	4 (10.0)	0	4 (10.0)/1 (2.5)/3 (7.5)
N	40	40	40	40	40

IOP, intraocular pressure.

injections of DEX over 2 years statistically significantly improved both CDVA and CRT at 12 and 24 months.[32]

Ten of the 15 treatment-naïve patients who were phakic at baseline did not undergo cataract surgery during the study. A subgroup analysis excluding those patients was conducted to evaluate their potential impact on the BCVA and CRT outcomes. The changes in mean BCVA and CRT from baseline were generally consistent with those of the overall treatment-naïve cohort, suggesting that DEX is an effective DME treatment, regardless of lens status.

The safety profile of DEX was acceptable and no unexpected adverse events were reported. Increased IOP was the most frequent treatment-emergent adverse event observed, consistent with previous report.[26] However, the proportion of patients who required IOP-lowering medications for increased IOP was lower in this analysis (≤22.2%) than in MEAD (≤41.5%).[25] It is also notable that no cases of elevated IOP recorded during the AUSSIEDEX study required intervention with laser or surgery, similar to what was reported in other investigations of DEX in clinical settings with 12-month follow-up.[30 31]

Potential study limitations include the fact that there was no set time by which phakic patients were required to undergo cataract surgery and some patients had not undergone cataract surgery by the end of the 12-month study. This could have caused vision to deteriorate and the BCVA letter gain achieved with DEX to be underestimated. Nonetheless, the change in BCVA from baseline reported in the subgroup of pseudophakic treatment-naïve patients was similar, suggesting that, over 12 months, DEX is an effective DME monotherapy in phakic and pseudophakic patients. The absence of minimal BCVA and CRT requirements at baseline should also be considered, as a more homogeneous population could potentially have led to greater and/or more consistent effects of DEX on BCVA and CRT across visits. However, this study was designed to reflect the broader population of patients encountered in typical clinics, compared with clinical trials.

In summary, DEX monotherapy was effective in treating DME in Australian clinical practice settings, regardless of lens status. There were no new, unexpected treatment-related adverse events during the study and treatment-emergent adverse events were manageable. The study findings indicate that DEX is an effective alternative treatment option for patients with treatment-naïve DME.

Correction notice This article has been amended since it was first published. In table 1, the indentations have been removed for two rows of the tables. Reference 4 has also been corrected.

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Data availability statement Data are available on reasonable request. AbbVie is committed to responsible data sharing regarding the clinical trials we sponsor. This includes access to anonymised, individual and trial-level data (analysis data sets), as well as other information (eg, protocols and Clinical Study Reports), as long as the trials are not part of an ongoing or planned regulatory submission. This includes requests for clinical trial data for unlicensed products and indications. This clinical trial data can be requested by any qualified researchers who engage in rigorous, independent scientific research, and will be provided following review and approval of a research proposal and Statistical Analysis Plan (SAP) and execution of a Data Sharing Agreement (DSA). Data requests can be submitted at any time and the data will be accessible for 12 months, with possible extensions considered. For more information on the process, or to submit a request, visit the following link: https://www.abbvie.com/our-science/clinical-trials/clinical-trials-data-and-information-sharing/data-and-information-sharing-with-qualified-researchers.html.

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