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Visual functioning and characterization of visual effects from SERENA-6, a Phase 3 study of switch to camizestrant from aromatase inhibitor while continuing CDK4/6 inhibitor at emergence of *ESR1* mutations during first-line therapy for patients with HR+/HER2– advanced breast cancer

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Objective

- To report a detailed analysis of visual effect AEs, results from a variety of ophthalmological assessments, and patient-reported visual functioning in the SERENA-6 trial

Conclusions

- Patient-reported visual functioning with camizestrant + CDK4/6 inhibitor was similar to the AI + CDK4/6 inhibitor arm
- Results from the ophthalmological assessments collectively demonstrated that there is no impact on ocular structure and function or visual acuity with camizestrant + CDK4/6 inhibitor treatment
- Photopsia (brief flashes of light in the peripheral vision) was the most common visual effect AE reported with camizestrant + CDK4/6 inhibitor, and 90% of events were mild (Grade 1)
- Together with the clinical efficacy of camizestrant + CDK4/6 inhibitor, and prior data showing that visual effects with this combination are brief, infrequent, with no or minimal impact on daily living,[4] these data support this combination as a potential new treatment strategy for patients with HR+/HER2– advanced breast cancer and emergent *ESR1*m during first-line AI + CDK4/6 inhibitor, ahead of disease progression

Plain language summary

Why did we perform this research?

- Camizestrant is a drug that blocks and destroys estrogen receptors, including mutated forms of those receptors, on cancer cells, thereby reducing their growth
- In SERENA-6, half of the patients in the study switched treatment from an aromatase inhibitor to camizestrant when an *ESR1* mutation was detected, and when their cancer was stable. Researchers found that switching to camizestrant significantly increased the average length of time before the cancer grew, spread, or got worse (known as progression-free survival). Patients also continued treatment with the CDK4/6 inhibitor that they were already taking
- Photopsia (brief flashes of light at the edge of vision) was reported in 31 of 155 patients who received camizestrant plus CDK4/6 inhibitor and 12 of 155 patients who received an aromatase inhibitor plus CDK4/6 inhibitor
- Here, we report more details of additional visual side effects of patients in SERENA-6, as well as results from eye examinations, and how patients rated the effects of visual side effects

How did we perform this research?

- Doctors performed different types of eye exams just before patients started taking trial treatments and as needed during the trial
- Patients in SERENA-6 were asked to complete a short questionnaire at regular intervals
  - The questionnaire was specifically designed to find out how visual side effects affected the patients' ability to function in their daily life, and about specific symptoms, such as eye pain

What were the findings of this research, and what are the implications?

- Patients' ability to function, including the ability to drive, was similar in those who received camizestrant plus CDK4/6 inhibitor and those who received an aromatase inhibitor plus CDK4/6 inhibitor
- Results from the eye exams show that camizestrant plus CDK4/6 inhibitor does not lead to permanent changes in the structure of the eye
- Visual side effects reported with camizestrant plus CDK4/6 inhibitor were mostly mild in severity and occurred early in treatment
- Results reported in this poster build on findings from other patient questionnaires in SERENA-6, which showed that visual side effects with camizestrant plus CDK4/6 inhibitor were infrequent, happened for a short time, and caused little or no bother
- Camizestrant plus CDK4/6 inhibitor could be a potential new treatment option for patients with hormone receptor-positive advanced breast cancer who had an *ESR1* mutation detected during initial treatment with aromatase inhibitor plus CDK4/6 inhibitor, and when their cancer was stable

Poster

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Introduction

- Camizestrant is a next-generation oral SERD and complete ER antagonist[1,2]
- The Phase 3 SERENA-6 trial assessed switching from an AI to camizestrant in the first-line setting while continuing CDK4/6 inhibitor, guided by the emergence of *ESR1*m in ctDNA, in patients with HR+/HER2– advanced breast cancer and no evidence of clinical or radiological progression[3]
  - Switching to camizestrant with continuation of CDK4/6 inhibitor resulted in a statistically significant improvement in PFS vs continuation of AI + CDK4/6 inhibitor (median 16.0 vs 9.2 months; hazard ratio 0.44 [95% CI, 0.31–0.60, *P*<0.0001])
  - Camizestrant + CDK4/6 inhibitor also delayed time-to-deterioration in GHS/QoL as measured by the EORTC QLQ-C30 (median 21.0 vs 6.4 months, hazard ratio 0.54 [95% CI, 0.34–0.84])[4]
- Photopsia (brief flashes of light in the periphery of vision) was the most commonly reported non-hematological AE in patients receiving camizestrant + CDK4/6 inhibitor[3]
- Prior patient-reported outcomes data from SERENA-6 demonstrate that visual effects with camizestrant + CDK4/6 inhibitor were typically brief (<1 minute/episode), occurred mostly in the morning or evening, and were infrequent (occurring ≤3 days per week), as measured by the VSAQ[5]
  - Patients reported that visual effects caused no or a low degree of bother, and had no or minimal impact on activities of daily living
- There is no evidence of structural effects on the eye or change in visual acuity attributable to camizestrant treatment[3]
- Consistent with clinical findings, nonclinical studies in rats support a reversible, pharmacological effect of camizestrant on retinal responses during light transitions in the absence of structural changes[6]
- We report a detailed analysis of visual effect AEs, ophthalmological assessments, and patient-reported visual functioning in SERENA-6

Methods

- SERENA-6 is a Phase 3, randomized, double-blind, placebo-controlled study that implemented *ESR1*m surveillance during first-line treatment with AI + CDK4/6 inhibitor in patients with HR+/HER2– advanced breast cancer. Patients with emerging *ESR1*m were randomized to continue AI + CDK4/6 inhibitor or switch to camizestrant + CDK4/6 inhibitor ahead of disease progression (NCT04964934)

Safety assessments

- The safety population included all patients who had received ≥1 dose of any trial treatment and was also used for patient-reported outcome analyses
- AEs were recorded continuously until 4 weeks after treatment discontinuation and were graded according to the NCI-CTCAE v5.0

Ophthalmologic assessments

- Ophthalmological examinations were conducted at baseline, where feasible, or up until Day 1 of Cycle 2, as clinically indicated during treatment, and at the treatment discontinuation visit. Per protocol, patients were considered for referral to an ophthalmologist for visual effects that were Grade ≥2 or limiting instrumental activities of daily life
- Assessments included: best corrected (manifest refraction) and uncorrected near and distance visual acuities; current glasses/lens prescription (if applicable); pupillary light reflex; extraocular muscle movements; confrontation visual fields; full anterior segment examinations with a slit lamp, including fluorescein or comparable vital staining of the cornea; intraocular pressure measurements; dilated fundoscopy exam, including the optic nerve and retina, unless medically contraindicated; and evaluation of dry eye per local standard
  - Optical coherence tomography was performed where locally accessible

Patient-reported vision-related health status

- Evaluation of vision-related health status as measured by the NEI-VFQ-25[7] was a predefined exploratory endpoint. The NEI-VFQ-25 is summarized in **Table 1**
- Adherence to the NEI-VFQ-25 was calculated for each timepoint and was defined as the number of patients with an evaluable questionnaire (≥1 subscale completed) divided by the total number of patients expected to complete the questionnaire at that timepoint

Table 1. Overview of the NEI-VFQ-25

Aspect	Description
Description of the NEI-VFQ-25	The NEI-VFQ-25[7] comprises 11 subscales, consisting of global vision rating, difficulty with near vision activities, difficulty with distance vision activities, limitations in social functioning due to vision, role limitations due to vision, dependency on another due to vision, mental health symptoms due to vision, driving difficulties, limitations with peripheral, color vision, ocular pain, as well as a general health rating question
Schedule of assessments	Patients completed the NEI-VFQ-25 at baseline (Day 1 of Cycle 1), every 6 months thereafter until treatment discontinuation, and at the treatment discontinuation visit
Statistics	Item scores were converted to a 0–100 scale, with a higher score representing better functioning. Items within each subscale were averaged together to create the subscale scores. The composite score was calculated by averaging the 11 vision-targeted subscales

Results

Patients

- In SERENA-6, 315 patients were randomized to receive camizestrant + CDK4/6 inhibitor (N=157) or AI + CDK4/6 inhibitor (N=158)
  - In both treatment arms, 155 patients received ≥1 dose of any study treatment and were followed-up for safety and patient-reported outcomes

Visual effects by AE reporting

- Of the patients reporting a visual effect AE, the majority were Grade 1 in both the camizestrant + CDK4/6 inhibitor arm (n=44/49) and the AI + CDK4/6 inhibitor arm (n=24/25) (**Table 1**)
  - A Grade 3 visual effect AE was reported in only 1 patient in the camizestrant + CDK4/6 inhibitor arm (photopsia, limiting instrumental activities of daily living). This event occurred at night in artificial light and was reversible in nature
- Visual effect AEs did not require monitoring, management with additional treatment, or specialist involvement
- There were no serious visual effect AEs in the camizestrant + CDK4/6 inhibitor arm; there was 1 serious visual effect AE in the AI + CDK4/6 inhibitor arm (visual impairment, Grade 1)
- The most commonly reported visual effect AE was photopsia, which was reported in 20.0% of patients in the camizestrant + CDK4/6 inhibitor arm and 7.7% of patients in the AI + CDK4/6 inhibitor arm (**Table 1**)
  - In either arm, ≥90% of these events were Grade 1
- Median time to first report of a visual effect AE was 8 days with camizestrant + CDK4/6 inhibitor and 23 days with AI + CDK4/6 inhibitor
- Visual effect AEs did not lead to treatment discontinuation in either treatment arm

Table 1. Summary of all visual effect AEs

	Camizestrant + CDK4/6 inhibitor (n=155)				AI + CDK4/6 inhibitor (n=155)			
AE, n (%)	Any Grade	Grade 1	Grade 2	Grade 3	Any Grade	Grade 1	Grade 2	Grade 3
Any	49 (31.6)	44 (28.4)	4 (2.6)	1 (0.6)	25 (16.1)	24 (15.5)	1 (0.6)	0
Photopsia	31 (20.0)	28 (18.1)	2 (1.3)	1 (0.6)	12 (7.7)	11 (7.1)	1 (0.6)	0
Vision blurred	11 (7.1)	9 (5.8)	2 (1.3)	0	11 (7.1)	11 (7.1)	0	0
Visual impairment	6 (3.9)	6 (3.9)	0	0	3 (1.9)	3 (1.9)	0	0
Diplopia	3 (1.9)	3 (1.9)	0	0	2 (1.3)	2 (1.3)	0	0
Photophobia	3 (1.9)	3 (1.9)	0	0	0	0	0	0
Visual perseveration	2 (1.3)	2 (1.3)	0	0	0	0	0	0

Table shows AEs regardless of causality. Patients with >1 visual effect AE (group term) were counted once in total values. Glare was not reported in patients from either arm.

Ophthalmological assessments

Visual acuity

- In either arm, the majority of patients with a baseline and ≥1 on-treatment assessment had a <1-line loss from baseline in best-correct visual acuity in both eyes, which was considered not to be a clinically meaningful change from baseline in visual acuity (**Table 2**)
  - Clinically significant changes (≥3-line loss) in visual acuity were rare, unilateral, nonprogressive, and reported in ≤6% patients in either treatment arm
- No patient experienced bilateral or progressive ≥3-line best-corrected visual acuity distance loss

Other ophthalmology assessments

- Of the patients who had a baseline and a post-baseline assessment, the majority had no clinically meaningful change from baseline when assessed using fundoscopy, slit lamp, pupillary light reflex test, extraocular muscle movement test, and optical coherence tomography (**Table 3**)
  - Clinically significant findings were generally rare, unilateral, nonprogressive, and occurred at similar frequencies in either treatment arm
- No patients had drug-related visual field defects (data not shown)
- There were no increases in intraocular pressure from baseline in either treatment arm
  - In patients receiving camizestrant + CDK4/6 inhibitor who were analyzed for change from baseline in intraocular pressure (n=30), mean (SD) change from baseline was −0.5 (2.4) mmHg in the left eye and −1.9 (6.2) mmHg in the right eye
  - In patients receiving AI + CDK4/6 inhibitor who were analyzed for change from baseline in intraocular pressure (n=32), mean (SD) change from baseline in intraocular pressure was −0.5 (3.1) mmHg in the left eye and −0.7 (2.9) mmHg in the right eye
- No ophthalmic abnormalities were reported as a serious AE, and no ocular events led to treatment discontinuation in either treatment arm

Table 2. Worst change from baseline in best-corrected visual acuity was not clinically meaningful in the majority of patients and was comparable between arms

	Camizestrant + CDK4/6 inhibitor		AI + CDK4/6 inhibitor	
	Left eye	Right eye	Left eye	Right eye
Number of patients with a baseline assessment and ≥1 post-baseline assessment, n	35	36	35	35
Patients with no change or a decrease in visual acuity, n (%)	32	31	29	30
<1-line loss*	27 (84.4)	26 (83.9)	22 (75.9)	23 (76.7)
1-line loss	3 (9.4)	2 (6.5)	5 (17.2)	5 (16.7)
2-line loss	0	2 (6.5)	1 (3.4)	1 (3.3)
≥3-line loss	2 (6.3)	1 (3.2)	1 (3.4)	1 (3.3)

Data are shown only for patients with a paired baseline and post-baseline assessment. Percentages are calculated from patients who had no change or a decrease in visual acuity.
*<1-line loss was considered no clinically meaningful change from baseline in visual acuity.

Table 3. Ophthalmological examinations showed no clinically meaningful changes in the majority of patients in both treatment arms

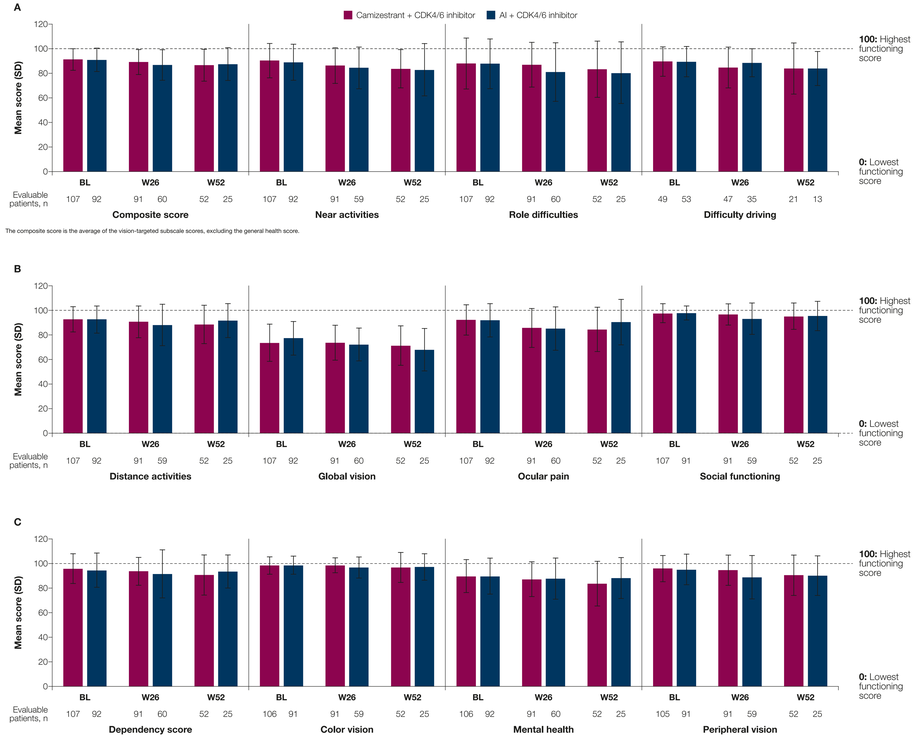
	Camizestrant + CDK4/6 inhibitor		AI + CDK4/6 inhibitor	
	Left eye	Right eye	Left eye	Right eye
Change between baseline and worst on-treatment assessment, n (%)				
Fundoscopy	39		38	
No clinically meaningful change	36 (92.3)		38 (100)	
Improvement	2 (5.1)		0	
Worsening	1 (2.6)		0	
Slit lamp examination	36		35	
No clinically meaningful change	31 (86.1)		33 (94.3)	
Improvement	0		1 (2.9)	
Worsening	5 (13.9)		1 (2.9)	
Pupillary light reflex test	36		32	
No clinically meaningful change	36 (100)	36 (100)	32 (100)	32 (100)
Extraocular muscle movement test	37		32	
No clinically meaningful change	37 (100)	37 (100)	32 (100)	32 (100)
Optical coherence tomography	31		33	
No clinically meaningful change	30 (96.8)	29 (93.5)	33 (100)	33 (100)
Improvement	1 (3.2)	2 (6.5)	0	0

Categories are based on worst on-treatment values comparable to baseline assessments. No change includes on-treatment values comparable to baseline assessments. Improvement includes abnormal, clinically significant baseline values normalizing or becoming non-clinically significant on treatment. Worsening includes normal or abnormal, non-clinically significant baseline values becoming abnormal and clinically significant on treatment.

Patient-reported vision-related health status

- At baseline, 69% of patients in the camizestrant + CDK4/6 inhibitor arm and 60% of patients in the AI + CDK4/6 inhibitor arm completed ≥1 subscale of the NEI-VFQ-25
- Adherence to the NEI-VFQ-25 remained broadly stable post-baseline and was similar between treatment arms
- Patient-reported vision-related health status, as measured by the NEI-VFQ-25 composite score, was stable over time (**Figure 1A**). Mean composite scores remained ≥86 across all timepoints and were comparable between treatment arms
- All other visual-related subscales of the NEI-VFQ-25, including difficulty driving, performing near activities, and role functioning were similarly stable over time and comparable between treatment arms (**Figures 1B and C**)

Figure 1. Patient-reported visual functioning scores, as assessed by the NEI-VFQ-25, were stable and comparable between arms



The composite score is the average of the vision-targeted subscale scores, excluding the general health score.

Abbreviations

AE, adverse event; AI, aromatase inhibitor; BL, baseline; CDK4/6, cyclin-dependent kinase 4/6; CI, confidence interval; ctDNA, circulating tumor DNA; EORTC, European Organisation for Research and Treatment of Cancer; ER, estrogen receptor; *ESR1*m, mutations in the estrogen receptor alpha gene; GHS, global health score; HER2–, human epidermal growth factor receptor 2-negative; HR+, hormone receptor-positive; NCI-CTCAE, National Cancer Institute Common Terminology Criteria for Adverse Events; NEI-VFQ-25, National Eye Institute-Visual Function Questionnaire-25; PFS, progression-free survival; QLQ-C30, Quality of Life Questionnaire Core 30; QoL, quality of life; SD, standard deviation; SERD, selective estrogen receptor degrader; VSAQ, Visual Symptom Assessment Questionnaire; W, week.

References

1. Scott JS, et al. *J Med Chem* 2020;63(23):13530–14559.
2. Lawson M, et al. *Cancer Res* 2023;83(23):3989–4004.
3. Bidard FC, et al. *N Engl J Med* 2025;393(6):569–580.
4. Mayer E, et al. *Ann Oncol* 2025. doi:10.1016/j.annonc.2025.10.006. Online ahead of print.
5. Park YH, et al. Poster 528P presented at ESMO 2025, October 17–21, Berlin, Germany.
6. Hamm G, et al. *Trans Oncol* 2025;62:102539. doi:10.1016/j.tranon.2025.102539. Online ahead of print.
7. Mangione CM, et al. *Arch Ophthalmol* 2001;119(7):1050–1058.

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