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A Phase 2 Study of Lurbinectedin Plus Durvalumab as Maintenance Therapy for ES-SCLC Following First-Line Induction Therapy

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Objective

- To evaluate the efficacy and safety of lurbinectedin plus durvalumab as first-line maintenance (1Lm) therapy in patients with extensive-stage small cell lung cancer (ES-SCLC) following induction with durvalumab plus etoposide-platinum chemotherapy

Study status

- The JZP712-203 trial is actively recruiting as of June 2026
- The trial will include clinical sites in the US, Canada, and Europe
- Approximately 70 patients will be screened, of whom approximately 50 will be enrolled and treated
- The primary analysis is planned to occur approximately 6 months after the first maintenance dose received by the last participant
- The anticipated study completion date is April 2028

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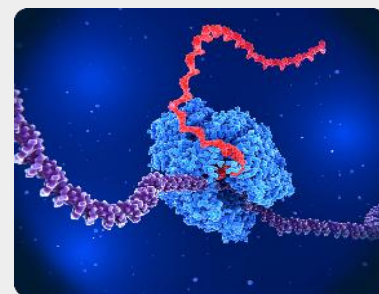
Background

- The IMpower133 and CASPIAN studies established immune checkpoint inhibitors (ICIs; atezolizumab and durvalumab) combined with chemotherapy as a first-line (1L) standard of care for ES-SCLC^{1,2}
- Although the incorporation of an ICI into 1L therapy has improved median overall survival (OS) to approximately 12 months compared with approximately 10 months with chemotherapy alone,³ the prognosis for ES-SCLC remains poor, and long-term survival is dismal⁴
- Lurbinectedin is an inhibitor of oncogenic transcription that exerts multiple mechanisms of action, including modulating the tumor microenvironment, thereby demonstrating synergy with immunotherapy (Figure 1)^{5,6}
- The randomized, controlled, phase 3 IMforte study (NCT05091567) demonstrated that the addition of lurbinectedin to the anti–programmed death-ligand 1 (PD-L1) ICI atezolizumab as maintenance therapy significantly and meaningfully improved progression-free survival (PFS) and OS vs atezolizumab alone in patients with ES-SCLC without progression after 1L induction therapy (Figure 2)⁷
 - The safety profile of the combination was manageable and consistent with the known profiles of each agent⁷
- These results led the US Food and Drug Administration and the European Commission to approve lurbinectedin plus atezolizumab as 1Lm treatment for patients with ES-SCLC in 2025 and 2026, respectively^{8,9}

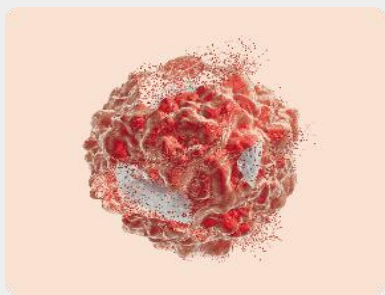
JZP712-203 (NCT07459634): Study rationale

- Durvalumab is an anti–PD-L1 inhibitor indicated for 1L treatment of ES-SCLC^{10,11}
- This study may provide insight into whether patients may benefit from lurbinectedin combined with another PD-L1 inhibitor (ie, durvalumab), which would be relevant given the widespread use of both PD-L1 inhibitors in the 1L setting
- The combination of lurbinectedin and durvalumab showed a manageable safety profile in relapsed ES-SCLC in a phase 2 trial¹²

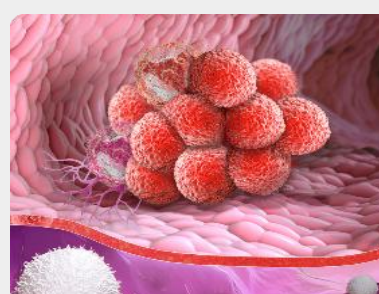
Figure 1. Lurbinectedin has multiple antitumor mechanisms of action



Inhibits DNA transcription
Binds to the minor groove of DNA, inhibiting transcription by RNA polymerase II and affecting DNA repair pathways^{8,13}



Induces tumor cell apoptosis
Induces double-stranded DNA breaks that trigger tumor cell apoptosis^{8,13}



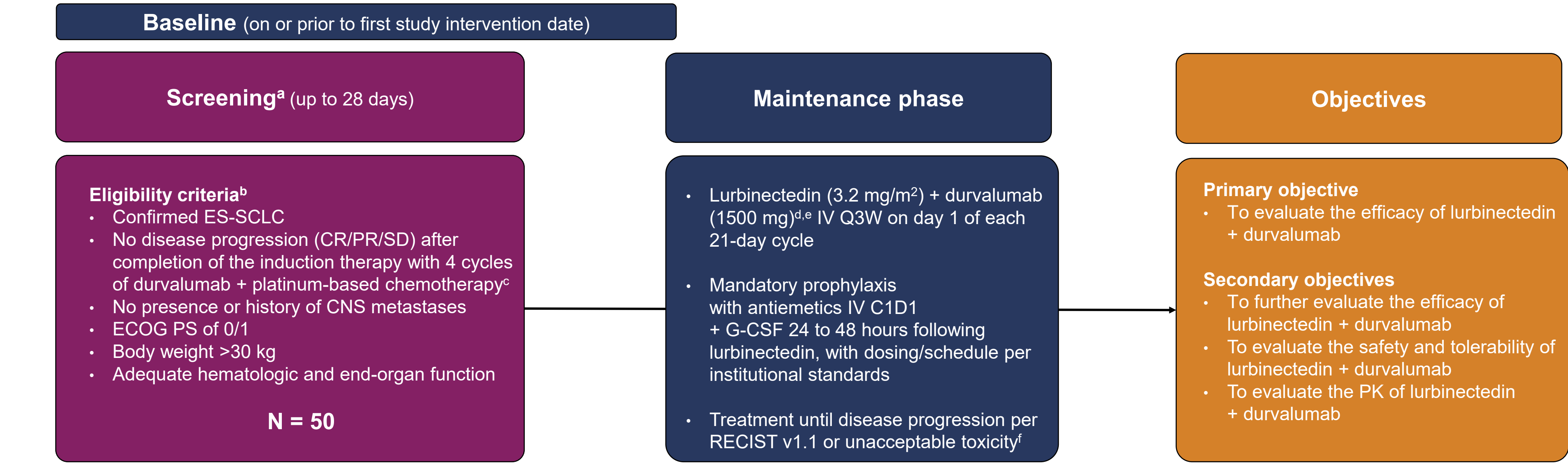
Modulates the tumor microenvironment

- Reduces immunosuppressive tumor-associated macrophages^{5,14}
- Increases the proliferation and infiltration of cytotoxic T cells/natural killer cells^{5,15}
- Promotes antigen presentation¹⁶
- Induces proinflammatory cytokines^{15,16}

Methods

Figure 3. Study design of the phase 2 JZP712-203 study

- JZP712-203 (NCT07459634) is a phase 2, multicenter, open-label, single-arm study evaluating the efficacy and safety of lurbinectedin plus durvalumab as maintenance therapy in patients with ES-SCLC whose disease has not progressed after 1L induction therapy (Figure 3)¹⁷



^aBaseline scans include a RECIST v1.1 tumor assessment scan and brain MRI or CT scan with contrast of the head.
^bProphylactic cranial irradiation is permitted per local standard of care after completion of induction treatment and is required to be completed before initiation of the maintenance phase.
^cAdministered per standard dose (administration of 3 cycles of durvalumab is acceptable if 4 cycles are not feasible during induction treatment).
^dThe durvalumab dose will be adjusted to 20 mg/kg Q3W for patients whose body weight falls below 30 kg.
^eDurvalumab will be administered first, followed by lurbinectedin. If lurbinectedin is discontinued due to toxicity, durvalumab may be continued; however, it must be switched to a Q4W dosing schedule.
^fTumor assessments will be performed every 6 weeks (±7 days) for the first 48 weeks following C1D1 of the maintenance phase, then every 9 weeks (±7 days) for 6 assessments and every 3 months (±7 days) thereafter, regardless of treatment delays, until radiographic disease progression per RECIST v1.1 occurs. Assessments will continue according to schedule after discontinuation of study intervention for reasons other than disease progression.
C1D1, cycle 1 day 1; CNS, central nervous system; cORR, confirmed objective response rate; CR, complete response; CT, computed tomography; ECOG PS, Eastern Cooperative Oncology Group Performance Status; ES-SCLC, extensive-stage small cell lung cancer; G-CSF, granulocyte colony-stimulating factor; IV, intravenous; MRI, magnetic resonance imaging; PFS, progression-free survival; PK, pharmacokinetics; PR, partial response; Q3W, every 3 weeks; Q4W, every 4 weeks; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1; SD, stable disease.

Table 1. Key eligibility criteria

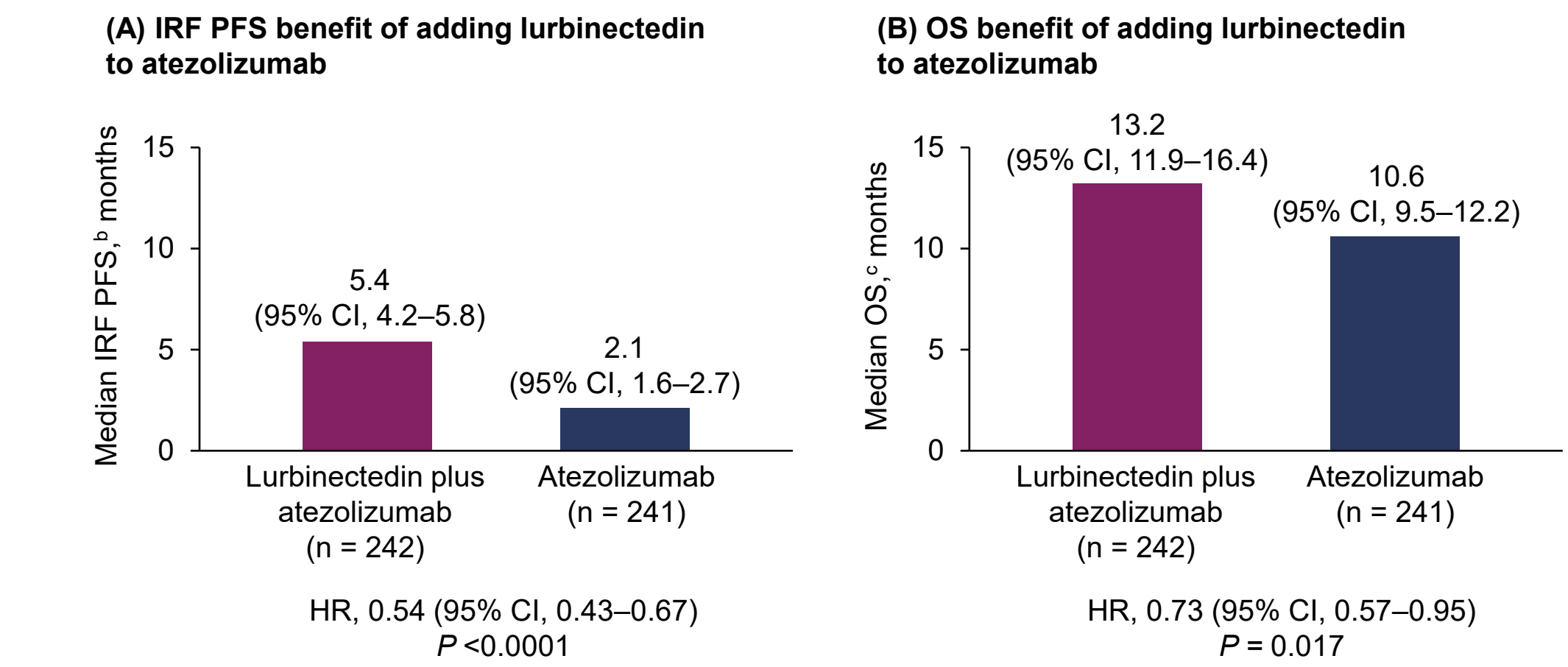
- Eligibility criteria for JZP712-203 are mostly aligned with those of the IMforte study (Table 1)⁷

 Inclusion criteria

- Aged ≥18 years or of the legal adult age per local standard at the time of signing the informed consent form
- Histologically or cytologically confirmed ES-SCLC according to the Veterans Administration Lung Study Group staging system
- Patients must have received 4 cycles of definitive platinum-based chemotherapy with durvalumab and have an ongoing CR or PR or have SD by RECIST v1.1 after completion of the induction therapy
 - Patients with ongoing CR or PR, or with SD per RECIST v1.1, after completing 4 cycles of definitive platinum-based chemotherapy combined with at least 3 cycles of durvalumab during the induction phase are eligible if administration of 4 cycles of durvalumab is not feasible for any reason
- Radiographic tumor assessment must have occurred ≤28 days prior to C1D1
- WHO/ECOG PS of 0 or 1
- Life expectancy ≥12 weeks as assessed by the treating physician
- Adequate hematologic and end-organ function for ≥7 days prior to dosing
- Toxicity related to prior induction cancer therapy or PCI must have resolved to baseline or grade ≤1 according to NCI CTCAE v5.0 or higher^a
- C1D1 dosing within 4 weeks from the day of administration of the last dose of induction treatment. Participants receiving PCI must be enrolled within 6 weeks of the last dose of induction treatment
- Body weight >30 kg

^aExcluding adverse events that are clinically nonsignificant and/or stable on supportive therapy and are not expected to interfere with treatment in the study.
^bExcluding malignancy treated with curative intent and with no known active disease ≥5 years before the first dose of study intervention and of low potential risk for recurrence, adequately treated nonmelanoma skin cancer or lentigo maligna without evidence of disease, or adequately treated carcinoma in situ without evidence of disease.
^cHistory of radiation pneumonitis in the radiation field (fibrosis) is permitted.
C1D1, cycle 1 day 1; CNS, central nervous system; CR, complete response; CT, computed tomography; ECOG PS, Eastern Cooperative Oncology Group Performance Status; ES-SCLC, extensive-stage small cell lung cancer; NCI CTCAE v5.0, National Cancer Institute Common Terminology Criteria for Adverse Events version 5.0; PCI, prophylactic cranial irradiation; PR, partial response; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1; SD, stable disease; WHO, World Health Organization.

Figure 2. Efficacy results from the phase 3 IMforte study comparing lurbinectedin plus atezolizumab vs atezolizumab alone as 1Lm therapy^{a,7}



^aBoth endpoints are measured from the time of randomization into maintenance therapy.
^bPer RECIST v1.1.
^cMedian time from induction C1D1 to randomization was 3.2-months in each arm.
1Lm, first-line maintenance; C1D1, cycle 1 day 1; ES-SCLC, extensive-stage small cell lung cancer; HR, hazard ratio; IRF, independent review facility–assessed; OS, overall survival; PFS, progression-free survival; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1.

Table 2. Trial endpoints measured from the start of 1Lm treatment

Primary endpoint

- PFS rate at 6 months per RECIST v1.1 by investigator assessment

Secondary endpoints

- PFS time per RECIST v1.1 by investigator assessment
- cORR per RECIST v1.1 by investigator assessment^a
- Frequency, severity, seriousness, and relatedness of AEs graded according to the NCI CTCAE v5.0 or higher
- Frequency of dose modification and study intervention discontinuations of any component of combination therapy
- Plasma concentrations of lurbinectedin

Exploratory endpoints

- Change in ctDNA from baseline during the maintenance phase
- Baseline AAG

^aThe maintenance-screening will serve as the RECIST v1.1 baseline.
1Lm, first-line maintenance; AAG, alpha-1 acid glycoprotein; AE, adverse event; cORR, confirmed objective response rate; ctDNA, circulating tumor DNA; NCI CTCAE v5.0, National Cancer Institute Common Terminology Criteria for Adverse Events version 5.0; PFS, progression-free survival; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1; SAE, serious AE.

Statistical analyses

- This single-arm study is designed for estimation, with no formal hypothesis testing; efficacy endpoints will be characterized by point estimates with 95% CIs. No formal interim analysis is planned
 - The remaining secondary and exploratory endpoints will be summarized descriptively
- The sample size of approximately 50 was selected for precision rather than power: in the Monte Carlo simulation assuming a true 6-month PFS rate of 40%, the central 95% empirical range (2.5th–97.5th percentiles) of the simulated Kaplan-Meier estimates was approximately 26%–54% (empirical half-width, 14 percentage points); across assumed true rates of 32%–56%, the empirical half-width ranged from 12.9 to 14.0 percentage points
- The efficacy and safety endpoints will be assessed in the safety analysis set, which will include all patients who receive ≥1 dose of durvalumab or lurbinectedin during the maintenance phase; confirmed objective response rate will be analyzed in the subset of patients with measurable disease at baseline per RECIST v1.1
 - The start and stop dates for adverse events can be imputed to calculate the duration of events
 - Censoring rules will be applied to the estimation of the distribution of the time-to-event endpoints
- The 6-month PFS rate—the Kaplan-Meier estimate of the probability of being alive and progression-free at 6 months—will be reported with its 95% CI (Greenwood variance, log-log transformation; Table 2)
 - Median PFS with quartiles (Qs; Q1, Q3) will be summarized separately for the secondary PFS-time endpoint (Brookmeyer-Crowley 95% CI)
- The confirmed objective response rate will be summarized by a binomial response rate with a 2-sided 95% exact CI

Clinical significance

- If positive, this trial will complement the phase 3 IMforte findings and support lurbinectedin as a broad, backbone-agnostic maintenance option for patients with ES-SCLC across standard first-line anti–PD-L1 regimens