TPS8657 Poster Session

FIRST-NEC (GFPC 01-2022): A multicenter phase II study evaluating the efficacy and safety of the combination of durvalumab with etoposide and platinum as first line treatment in patients with advanced large-cell neuroendocrine lung carcinomas (LCNECs).

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Background: LCNECs of the lung are rare lung tumors (2%) with difficult histopathological diagnosis (70-80% confirmation rate after centralized review). Platinum–based regimen is currently the recommended first-line treatment for advanced LCNECs. However it results in poor median progression-free survival (PFS) and overall survival (OS) of 5 months and 7.7 months, respectively. Retrospective studies have suggested efficacy of immune checkpoint inhibitors against LCNECs with significantly prolonged OS. In addition, the CASPIAN trial demonstrated the superiority of durvalumab plus platinum-etoposide over chemotherapy alone in patients with extensive-stage neuroendocrine small cell lung cancer, with an acceptable toxicity profile. **Methods:** This ongoing single-arm phase II trial is designed to evaluate the efficacy and safety of durvalumab in combination with platinum-etoposide as first line treatment in pts with locally diagnosed advanced LCNEC. Key selection criteria are age $\geq$ 18 years, ECOG PS 0-1, measurable disease (RECIST 1.1) and locally advanced (Stage III) ineligible for loco-regional therapy or metastatic (Stage IV). Central confirmation of the histopathological diagnosis will be performed for all pts at the start of treatment. All pts will receive 4 cycles of induction with durvalumab 1500mg, platinum (either carboplatin AUC5 or cisplatin 80mg/m^2 at D1) and etoposide 100mg/m^2 (D1-D3), repeated every 3 weeks. Durvalumab 1500mg will be continued alone every 4 weeks for a maximum of 24 additional cycles or until disease progression or unacceptable toxicity. The primary endpoint is to determine, in pts with confirmed diagnosis, 12-month progression-free rate (12M-PFR) as per central radiological review. Secondary endpoints include PFS, OS and safety. Radiological criteria will be described using the RECIST 1.1 both as per investigator's assessment and as per central radiological review. Biomarkers will be studied as predictive and prognostic factors of efficacy. Efficacy will be assessed sequentially every ten pts using a Bayesian approach. Analogous to a frequentist approach from an A'Hern-Fleming single-stage design, 51 evaluable pts will be enrolled. A futility stopping rule will stop the trial if there is a high probability (>80%) that the 12M-PFR is less than or equal to P0 (15%). Finally, a trial emulation will be performed as an exploratory analysis to assess PFS and OS compared to an external control arm by using real-world data from the ESME database. Since the start of recruitment (June 2024), 13 patients with a confirmed diagnosis have been included. Clinical trial information: NCT06393816. Research Sponsor: French ministry of health / French National Cancer Institute (INCa); PHRC-K23-033; Astrazeneca; Not applicable (drug supply).