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TPS2674 **Poster Session**

A non-inferiority randomized phase III trial of standard immunotherapy versus reduced dose intensity in responding patients with metastatic cancer: MOIO study.

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Background: Immunotherapy (IO) is increasingly used for treating various metastatic cancers. With respect to the pharmacologically-active levels of IO drugs and their pharmacokinetics features, standard scheduling lead to plasma exposures largely exceeding the thresholds associated with target engagement. Indeed, phase I studies have shown that saturation of the target can persist far beyond the serum IO drugs half-life. *In silico* modeling has suggested that alternate scheduling (i.e. 3-monthly dosing) could be performed without compromising efficacy. Indeed, prolonged IO half-lives, time-varying clearance plus plasma concentrations far above the threshold associated with maximal target-engagement, suggest that the rhythm of IO administration could be slowed down. A phase II showed that extending IO dosing intervals did not compromise efficacy, while reducing toxicity in metastatic renal cell cancer. **Methods:** This non-inferiority, randomized, French national multicenter (36 centers involved) phase III study (NCT05078047) aims to compare the standard scheduling of a variety of IO drugs VS. 3-monthly scheduling in adult patients with metastatic cancer in partial (PR) or complete response (CR) after 6 months of standard IO dosing (except melanoma in CR). The main objective is to demonstrate the non-inferiority in Progression-Free Survival (PFS) of the reduced intensity group compared to the standard regimen. Secondary objectives are cost-effectiveness, quality of life, anxiety and fear of relapse, response rate, overall survival, and toxicity. A 1:1 randomization by minimization will be conducted on the following stratification factors: therapy line (first line vs others), tumor type, IO type (anti-PD-1 vs anti-PD-L1) and response status (PR, CR). A total of 646 pts will be randomized to get the 498 events necessary to prove non-inferiority between groups. The main analysis will conclude that reduced dose intensity is non-inferior to standard scheduling if the hazard ratio for PFS, estimated by a Cox model after adjustment for stratification factors, is significantly lower than the predefined 1.30 non-inferiority margin. In order to minimize the number of patients exposed to suboptimal treatment, an independent data monitoring committee will specifically review the efficacy data and recommend the early termination of the trial if lack of efficacy is evidenced. Ancillary studies of pharmacokinetics and immune-monitoring will be conducted to provide mechanistic insights supporting the clinical outcomes observed in both groups. **Conclusion:** Should the hypothesis of non-inferiority with an IO reduced dose intensity be validated, alternate scheduling could preserve efficacy while being cost-effective and allowing a reduction of the toxicity, with an increase in patient's quality of life. Clinical trial information: NCT05078047. Research Sponsor: Institut National du Cancer France.