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Feasibility and reproducibility of PD-L1 assessment within CARE1: A phase III, randomized, biomarker-driven pragmatic trial to optimize first-line treatment in patients (pts) with metastatic clear-cell renal cell carcinoma (mRCC)

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Background

Dual immunotherapy (ICI) or ICI plus tyrosine kinase inhibitors (TKIs) is standard of care for first-line mRCC. The CARE1 trial aims to demonstrate superiority of dual ICI in PD-L1–positive (PD-L1+) disease, and of ICI-TKI in PD-L1–negative (PD-L1-) disease. Reporting of PD-L1 status has been inconsistent across pivotal trials, hampering its implementation. We assessed feasibility and reproducibility of concurrent local and centralized PD-L1 testing within the CARE1 trial.

Methods

Treatment-naïve pts with intermediate/poor risk mRCC were randomized to either dual ICI or ICI plus TKI. PD-L1 positivity was defined as a tumor score (TPS) ≥1% within representative slides (highest nucleolar grade, ≥100 viable tumor cells, no necrosis). Local staining was performed using local antibodies, central testing used DAKO 22C3 (PharmDx). The main endpoint was the rate of major discordances, defined as reclassification of pts from PD-L1+ to PD-L1- or vice-versa. Minor discordances were defined as changes in PD-L1 TPS within PD-L1+ pts.

Results

A total of 308 pts were included (primary tumor in 71%, metastases in 29%). Histological grade was ISUP 2 in 27%, 3 in 32%, 4 in 41% of pts; sarcomatoid/rhabdoid features reported in 25%, necrosis in 42%. Main local PD-L1 antibodies used were 22C3 in 55% of pts, SP263 (Ventana) and QR1 (Diagomics) 14% each. All pts had local PD-L1 testing, of whom 99% had successful central testing. The proportion of PD-L1+ pts was 45% by local and 43% by central testing; overall concordance was 90% for PD-L1 positivity. Among the major discordances, reported in 10% of pts, the false positive rate was 6% and the false negative rate 4%. Minor discordances were reported in 23%. Discordance rates were not affected by biopsy site, pathological features, antibody type.

Conclusions

Local PD-L1 assessment within the CARE1 trial achieved high reproducibility, regardless of antibody type, using standardized operating procedures. These data support the use of local PD-L1 assessment as stratification factor in the CARE1 trial, and further applicability to routine practice.

Clinical trial identification

EUCT: 2023-503317-29-00; NCT06364631.

Legal entity responsible for the study

Gustave Roussy.

Funding

European Union’s Horizon Europe research and innovation program under grant agreement No 101104801; National Cancer Institute in France PHRC; Gustave Roussy Foundation-Cris Cancer Foundation; Rising Tide.

Disclosure

R. Flippot: Financial Interests, Institutional, Advisory Role: Astellas, Ipsen, Johnson & Johnson, Bayer, Merck Serono, BMS, MSD, Pfizer, Eisai, Novartis; Financial Interests, Institutional, Coordinating PI: Bayer. N. Rioux-Leclercq: Financial Interests, Personal, Invited Speaker, Paid conferences: Amgen, AstraZeneca, BMS, Ipsen, Janssen, MSD; Financial Interests, Personal, Advisory Role: Merck-Pfizer, AstraZeneca, BMS, Ipsen. S. Foulon: Financial Interests, Personal, Advisory Board, Participation to the advisory board (statistical advice) of an epidemiological study performed by Gilead on real world data (medico-administrative data): Review and validation of the study protocol, validation of the study population, as well as the review and validation of the results and of the study report: Gilead.: Gilead. B. Melichar: Financial Interests, Personal, Advisory Board: Roche, BMS, MSD, Novartis, Merck Serono, Eli Lilly, Pfizer, AstraZeneca. S. 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