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Final efficacy data and biomarker analysis from the clear cell cohort of CALYPSO

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Background

CALYPSO is a phase II trial evaluating durvalumab (D), savolitinib (S) and tremelimumab (T) in previously treated advanced renal cell carcinoma (RCC). In this study, these agents were evaluated alone or in combination. We previously reported the interim analysis of response rates and progression-free survival (PFS). This abstract presents the final overall survival analysis (OS) in the clear cell RCC cohort.

Methods

A multinational, open-label, randomised phase II study in patients with advanced RCC previously treated with VEGF-targeted therapy but naïve to immune checkpoint and MET inhibitors. Patients were randomised to D, S DT or DS. The primary endpoint was confirmed response rate (cRR) with a threshold of ≥50% for further evaluation, which was not achieved. DNA alterations were assessed using Foundation One. KIM1, RNA-based analysis and PD-L1 in tumor cells, immune cells and combined between D and DS/DT are ongoing.

Results

From 2017 to 2021, 138 patients were randomised: D (N=39), S (N=21), DT (N=39), DS (N=39). Median age was 62 years (range: 28-85). cRRs were: D=10%, DT=28%, DS=13% (S=5%, closed early). Median duration of response was D=9.8 months, DT=19.4 months and DS=13.3 months. Twelve-month PFS rates were D=28% (95% CI: 15%–42%), DT=33% (95% CI: 19%–48%), and DS=20% (95% CI: 9%–34%). With a minimum follow-up of 3 years, median OS was D=25.8 months, DT=24.2 months, DS=16.3 months. A comparison of D vs DT and D vs DS showed HRs of 0.864 (80%CI: 0.607-1.229) and 1.549 (80%CI: 1.108-2.165), respectively. In the MET driven subgroup (N=17) OS HR for S (S+DS) vs non-S (D+DT) was 0.342 (80%CI: 0.154-0.761). Median tumor mutational burden (TMB) was 2.5 mutations/Mb (N=62) with no clear association with outcomes. Exploratory PD-L1analysis also appeared non-discriminatory. KIM1 and RNA-based analyses comparing D vs DS and DT are ongoing.

Conclusions

S did not appear to improve outcomes in ccRCC, although the MET driven exploratory subset requires further validation. While response rates for DT were higher than D alone, the predefined requirements were not met. Other endpoints such as OS were not discriminatory compared to D monotherapy.

Clinical trial identification

NCT02819596.

Legal entity responsible for the study

Queen Mary University of London.

Funding

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Disclosure

J. Larkin: Financial Interests, Personal, Other, Consultancy: Incyte, iOnctura, Apple Tree, Merck, BMS, Eisai, Debipharm, Pfizer, Novartis, MSD, Iovance Biotherapeutics, Boston Biomedical, YKT Global, Immunocore; Financial Interests, Personal, Other, Honorarium: touchIME, touchEXPERTS, Royal College of Physicians, Pfizer, Novartis, Incyte, Merck, Pfizer, Roche, iOnctura, Dynavax, CRUK, GSK, BMS; Financial Interests, Personal, Invited Speaker, Speaker Fee: BMS, Pfizer, Roche, Pierre Fabre, AstraZeneca, Novartis, EUSA Pharma, MSD, Merck, GSK, Ipsen, Aptitude, Eisai, Calithera, Ultimovacs, Seagen, eCancer; Financial Interests, Institutional, Funding: BMS, MSD, Novartis, Pfizer, Achilles, Roche, Nektar, Covance, Immunocore, Pharmacyclics, Aveo. B. Perez Valderrama: Financial Interests, Personal, Advisory Board: Pfizer, Astellas Pharma, Bristol-Myers-Squibb, Ipsen, EUSA Pharma, Merck, MSD, AstraZeneca, AAA, Recordati, Bayer; Financial Interests, Personal, Invited Speaker: Bristol-Myers-Squibb, Bayer, MSD, Merck, Pfizer, Astellas Pharma, AAA, Almirall pharma, Astra-Zeneca; Other, Other, Travel/accomodations: Bristol--Myers-Squibb, Pfizer, Roche, Astellas Pharma, MSD, Merck. A. Rodriguez-Vida: Financial Interests, Personal, Invited Speaker: Roche, BMS, Johnson & Johnson, ASTRAZENECA, IPSEN; Financial Interests, Personal, Advisory Board: MSD, Pfizer, ASTELLAS, BAYER, MERCK. J. Puente: Financial Interests, Personal, Advisory Board: Astellas, AstraZeneca, Janssen, MSD, Pfizer, Eisai, Ipsen, Roche, BMS, Merck, Novartis, Gilead; Financial Interests, Personal, Invited Speaker: Astellas, AstraZeneca, Janssen, MSD, Bayer, Pfizer, Eisai, Roche, BMS, Merck; Financial Interests, Institutional, Research Grant: Astellas, Roche, Merck, Pfizer; Other, Other, Travel expenses: AstraZeneca, Ipsen. T.B. Powles: Financial Interests, Personal, Advisory Board: AstraZeneca, Bristol Myers-Squibb, Exelixis, Incyte, Ipsen, Merck, Novartis, Pfizer, Seattle Genetics, Merck Serono, Astellas, Johnson & Johnson, Eisai, Roche, MSD; Financial Interests, Personal, Other, Travel/Accommodation/Expenses: Roche, Pfizer, MSD, AstraZeneca, Ipsen; Financial Interests, Personal, Other, Sponsorship for Uromigos Podcast: Mashup Ltd; Financial Interests, Institutional, Other, honoraria: Gilead; Financial Interests, Institutional, Research Grant: AstraZeneca, Roche, Bristol Myers-Squibb, Exelixis, Ipsen, Merck, MSD, Seattle Genetics, Novartis, Pfizer, Merck Serono, Astellas, Johnson & Johnson, Eisai; Financial Interests, Institutional, Other, Honoraria: Gilead. C. Suarez Rodriguez: Financial Interests, Personal, Advisory Board: Astellas, AstraZeneca, Bristol Myers Squibb International, Ipsen, MSD, MSD; Financial Interests, Institutional, Advisory Board: Astellas, AstraZeneca, Bristol Myers Squibb International, Ipsen, MSD, MSD; Financial Interests, Personal, Other, Travel and accommodation: Bayer; Financial Interests, Personal, Invited Speaker: Bristol Myers Squibb International, Ipsen, MSD; Financial Interests, Institutional, Invited Speaker: Bristol Myers Squibb International, Ipsen, MSD; Financial Interests, Institutional, Research Grant: Ipsen, Pfizer, Bristol Myers Squibb International, Roche, MSD. All other authors have declared no conflicts of interest.