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Alliance A092204: Phase II Study of Cabozantinib in Combination with Cemiplimab versus Cabozantinib in Adolescents and Adults with Adrenocortical Cancer

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BACKGROUND

Systemic chemotherapy with etoposide, doxorubicin, and cisplatin, in combination with the adrenolytic agent, mitotane is the current standard of care for advanced adrenocortical carcinoma (ACC). Toxicities are frequent, and outcomes are poor, underscoring the need for more effective treatment combinations. It is known that cabozantinib (cabo) monotherapy and anti-PD-1 monotherapy have meaningful activity in ACC; thus, combination of cabo with the anti-PD-1 therapy cemiplimab (REGN2810; cemi) may provide synergy. This randomized phase II trial evaluates whether cabo+cemi improves progression-free survival (PFS) versus cabo alone.

METHODS

Patients aged ≥12 years with locally advanced unresectable or recurrent/metastatic ACC, with measurable disease (RECIST v1.1), performance status ECOG 0–2 (≥18 years), Lansky ≥50 (12-<16 years), or Karnofsky ≥50 (16–<18 years), and body surface area ≥1.2 m^2 are eligible. Up to 3 prior lines of systemic therapy are allowed and treatment-naïve patients are eligible. Patients who received mitotane ≤6 months prior to registration must have discontinued mitotane and have a level <2 mg/L to be eligible due to interactions with cabo. A total of 48 patients (to achieve 46 evaluable) will be randomized 1:1 to cabo (Arm A) or cabo+cemi (Arm B) using Pocock–Simon dynamic allocation, stratified by prior systemic therapy (naïve vs ≥1 line) and corticosteroid-producing status (yes vs no);

crossover from Arm A to Arm B is permitted at disease progression. The primary endpoint is PFS (time from registration to progression or death) compared between arms in an intention-to-treat population. The design hypothesizes that cabo+cemi will result in meaningfully superior PFS of at least 10 months versus 5 mo with cabo alone (HR 0.5, α=0.10, 80% power). Secondary endpoints include safety and tolerability, objective response, duration of objective response, time to progression, and overall survival with cabo-cemi.

RESULTS

Enrolment is ongoing.

CONCLUSIONS

Clinical trial identification: NCT06900595

Support: U10CA180821, U10CA180882, UG1CA233331, UG1CA189822, UG1CA233180, UG1CA233339
https://acknowledgments.alliancefound.org

ABSTRACT ID #36396