389 PHASE II OF CD40 AGONISTIC ANTIBODY SOTIGALIMAB (APX005M) IN COMBINATION WITH NIVOLUMAB IN SUBJECTS WITH METASTATIC MELANOMA WITH CONFIRMED DISEASE PROGRESSION ON ANTI-PD-1 THERAPY

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Background A significant number of melanoma patients treated with anti-PD-1 alone or in combination with anti-CTLA-4 have transient or no response to treatment. Sotigalimab is a CD40 agonist antibody with unique epitope specificity and Fc receptor binding profile for optimal therapeutic application. Preclinical studies suggest that sotigalimab can be combined with PD-1 blockade to trigger effective anti-tumor immunity. We conducted a multi-center, open label, Phase Ib-parallel arm phase II trial (NCT03123783) to evaluate the combination of sotigalimab with nivolumab in subjects with anti-PD-1/PD-L1 refractory metastatic melanoma.

Methods The study objective was to evaluate the efficacy and safety of sotigalimab in combination with nivolumab in anti-PD-1/PD-L1 refractory advanced melanoma patients. Subjects received sotigalimab (0.3mg/kg) combined with nivolumab (360mg) every 3 weeks. Thirty-eight subjects with unresectable or metastatic melanoma who had confirmed progressive disease during treatment with anti-PD-1 therapy (documented by 2 consecutive tumor assessments) were enrolled (evaluable for safety) and 33 subjects were evaluable for efficacy.

Results Six subjects had PR (including one unconfirmed PR) for an ORR of 18%. The mDOR was 18.7 months. Two subjects with PR received treatment for >2 years. Three of the six responding subjects remain off all therapy for ≥26 months, and one patient required stereotactic radiosurgery to a single brain lesion ten months after stopping therapy and has not required additional local or systemic therapy since. Three additional subjects had prolonged SD (12.6, 7.6, 6.2 months). The DCR was 48% and 33% of subjects experienced reduction in target lesions. Efficacy was observed in patients regardless of their tumor PD-L1 expression. The overall safety profile of the combination is consistent with the profiles of individual agents. The majority of AEs observed were of mild to moderate intensity (CTCAE Grade ≤2). The most commonly observed AEs were: pyrexia, chills, nausea, fatigue, pruritus, transaminitis, headache, asthenia, myalgia, rash, vomiting and arthralgia. There were no Grade 4 or 5 AEs related to study drugs. There were no treatment discontinuations due to AEs.

Conclusions The combination of sotigalimab and nivolumab demonstrated treatment benefit (tumor response or prolonged disease control) in anti-PD-1/PD-L1 refractory melanoma patients with an overall favorable safety and tolerability profile. Notably, a subset of patients remain in response off treatment for ≥26 months. These results warrant further study of this combination in advanced, refractory melanoma.

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Trial Registration NCT03123783

Ethics Approval This study was approved by the Institutional Review Boards at Yale University (#20170300), University of Nebraska Medical Center (#543-18-CB) and The Hospital Regional de Málaga (#19.03.1341E1-GHM).

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