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POSTER ABSTRACTS

623.MANTLE CELL, FOLLICULAR, AND OTHER INDOLENT B CELL LYMPHOMAS: CLINICAL AND EPIDEMIOLOGICAL

Traverse: A Phase 2, Open-Label, Randomized Study of Acalabrutinib in Combination with Venetoclax and Rituximab in Patients with Treatment-Naive Mantle Cell Lymphoma

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Background and Significance: Despite advances in treatment for mantle cell lymphoma (MCL), no curative option exists. Currently, the majority of patients with treatment-naive (TN) MCL receive chemoimmunotherapy, which can result in prolonged remissions, but is associated with significant toxicity. Almost all patients inevitably relapse, and therefore, frontline chemotherapy-free options are being increasingly explored. Acalabrutinib is a highly selective, second-generation Bruton tyrosine kinase inhibitor (BTKi) approved for the treatment of adult patients with relapsed/refractory (R/R) MCL. In a phase 1b study in patients with TN MCL, acalabrutinib in combination with venetoclax and rituximab (AVR) demonstrated high rates of clinical and molecular response with an acceptable toxicity profile, supporting its continued development as a chemotherapy-free treatment option (Wang et al. *Blood*. 2021; Wang et al. *Blood*. 2022). Furthermore, the occurrence of complete responses (CRs) with clearance of minimal residual disease (MRD) in MCL clinical trials suggests that treatment may be stopped in these patients, as observed in patients with chronic lymphocytic leukemia who received combination therapy with venetoclax and rituximab.

Study Design and Methods: TrAVeRse (NCT#05951959) is a phase 2, open-label, randomized, multicenter, international study of AVR in patients with TN MCL. Patients aged ≥18 years with an Eastern Cooperative Oncology Group performance status of 0-2 (3 if due to lymphoma), and Ann Arbor stage II, III, or IV disease are eligible. Key exclusion criteria are active central nervous system involvement by lymphoma or leptomeningeal disease, severe/life-threatening illness or medical condition, clinically significant cardiovascular disease, stroke, or intracranial hemorrhage within 6 months of enrollment, and any active uncontrolled infection.

Approximately 125 patients will be screened to achieve a study population of 100 patients. During the induction phase, patients will receive oral acalabrutinib 100 mg twice daily (BID) in 28-day cycles for 13 cycles, starting at cycle 1; oral venetoclax once daily, starting at cycle 2 at a dose of 20 mg daily, with ramp-up to a maximum of 400 mg daily over 5 weeks for a total of 12 cycles; and intravenous rituximab 375 mg/m ^{2} on day 1 of every cycle for 12 cycles, starting at cycle 1. Patients who complete 13 cycles of AVR induction will be centrally tested for MRD status and continue to receive acalabrutinib 100 mg BID for 1 additional cycle (cycle 14) while awaiting disease response assessment and MRD results. Patients who achieve an MRD-negative CR (in peripheral blood at a threshold of 10^{-5}) at the end of induction will be randomly assigned in a 1:1 ratio to either continue to receive acalabrutinib 100 mg BID or to observation from cycle 15. Randomization will be stratified according to the simplified MCL International Prognostic Index [sMIPI] score (low [score, 0-3] and intermediate risk [4-5] vs high risk [6-11]), histologic features (blastoid or pleomorphic vs classical histology), and *TP53* status (mutated vs unmutated). Those with an MRD-positive CR, partial response (PR), or stable disease (SD) at end of induction will continue to receive acalabrutinib 100 mg BID until disease progression, death, or unacceptable toxicity. Patients who progress during observation may be retreated with acalabrutinib 100 mg BID at relapse.

The primary endpoint of this study is the MRD-negative CR rate at the end of AVR induction (ie, end of cycle 13). Secondary endpoints include MRD-negative CR rate at any point during the study, objective response rate and CR rate, duration of response, time to next treatment, progression-free survival, event-free survival, overall survival, safety, and tolerability. The

study will also assess the feasibility of response-adapted treatment cessation for those who achieve MRD-negative CR after AVR induction and the efficacy of acalabrutinib retreatment in the subgroup of patients randomized to observation who subsequently relapse. Patients will be followed for 36 months post last patient randomized. Enrollment is planned to begin Q3 of 2023 including sites in North America, Australia, and Europe.

Summary: This study will evaluate the efficacy of AVR, a chemotherapy-free triplet combination therapy, in patients with TN MCL.

Disclosures Hawkes: *Novartis:* Membership on an entity's Board of Directors or advisory committees, Other; *Merck Sharpe & Dohme:* Membership on an entity's Board of Directors or advisory committees; *Janssen:* Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *Beigene:* Other; *Specialised Therapeutics:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Merck KgA:* Research Funding; *Regeneron:* Speakers Bureau; *Gilead:* Membership on an entity's Board of Directors or advisory committees; *Astra Zeneca:* Membership on an entity's Board of Directors or advisory committees, Other: Travel Expenses, Research Funding, Speakers Bureau; *Antengene:* Membership on an entity's Board of Directors or advisory committees; *Roche:* Membership on an entity's Board of Directors or advisory committees, Research Funding; *Bristol-Myers Squibb:* Membership on an entity's Board of Directors or advisory committees, Research Funding. **Fletcher:** *AstraZeneca:* Current Employment, Current equity holder in publicly-traded company; *CRCTU, University of Birmingham:* Ended employment in the past 24 months. **Wood:** *University Hospitals Sussex NHS Foundation Trust:* Ended employment in the past 24 months; *Vanguard Investments Funds ICVC:* Current equity holder in publicly-traded company; *AstraZeneca:* Current Employment, Current equity holder in publicly-traded company. **Meyer:** *AstraZeneca:* Current Employment, Current equity holder in publicly-traded company. **Rule:** *AstraZeneca:* Current Employment. **Zhang:** *GRAIL:* Ended employment in the past 24 months; *Illumina:* Current equity holder in publicly-traded company; *AstraZeneca:* Current Employment. **Wang:** *MJH Life Sciences:* Honoraria; *MD Education:* Honoraria; *Meeting Minds Experts:* Honoraria; *Medscape:* Honoraria; *IDEOlogy Health:* Honoraria; *i3Health:* Honoraria; *Genmab:* Honoraria, Research Funding; *Kite, a Gilead Company:* Consultancy, Honoraria, Other: Travel, Research Funding; *Janssen:* Consultancy, Honoraria, Research Funding; *InnoCare:* Consultancy, Research Funding; *Merck:* Consultancy, Honoraria; *Eli Lilly and Company*: Consultancy, Research Funding; *Pharmacyclics:* Consultancy, Honoraria, Research Funding; *Dava Oncology:* Honoraria, Other: Travel; *Eastern Virginia Medical School:* Honoraria; *DTRM Biopharma (Cayman) Limited:* Consultancy; *Pepromene Bio:* Consultancy; *Parexel:* Consultancy; *Oncternal:* Consultancy, Research Funding; *Miltenyi Biomedicine:* Consultancy; *Milken Institute:* Consultancy; *AbbVie:* Consultancy, Honoraria; *Genentech:* Consultancy, Research Funding; *Bantam Pharmaceutical:* Honoraria; *VelosBio:* Consultancy, Research Funding; *CAHON:* Honoraria; *Bristol Myers Squibb:* Consultancy, Honoraria; *BioInvent:* Consultancy, Honoraria, Research Funding; *Leukemia & Lymphoma Society:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees; *BeiGene:* Consultancy, Honoraria, Research Funding; *Be Biopharma:* Consultancy; *Deciphera:* Consultancy; *Amphista Therapeutics Limited:* Consultancy; *Acerta Pharma:* Consultancy, Honoraria, Research Funding; *Celgene:* Other: Travel, Research Funding; *CSTone:* Consultancy; *OncLive:* Honoraria; *Moffit Cancer Center:* Honoraria; *AstraZeneca:* Consultancy, Honoraria, Other: Travel, Research Funding; *ADC Therapeutics America:* Consultancy; *Oncology Specialty Group:* Honoraria; *Nurix:* Honoraria; *NIH:* Honoraria; *Physicians Education Resources (PER):* Honoraria, Other: Travel; *Practice Point Communications (PPC):* Honoraria; *Studio ER Congressi:* Honoraria; *Physicians Education Resources:* Honoraria; *Practice Point Communications:* Honoraria; *Pharmacyclics:* Honoraria; *Loxo Oncology:* Consultancy, Research Funding; *Scripps:* Honoraria; *WebMD:* Honoraria; *Genentech:* Consultancy, Research Funding; *Juno Therapeutics:* Research Funding; *Molecular Templates:* Research Funding; *Vincerx:* Research Funding; *Anticancer Association:* Honoraria; *BGICS:* Honoraria; *Clinical Care Options:* Honoraria; *Epizyme:* Consultancy, Honoraria; *Hebei Cancer Prevention Federation:* Honoraria; *Imedex:* Honoraria; *TS Oncology:* Honoraria; *Mumbai Hematology Group:* Honoraria; *OMI:* Honoraria.

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