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POSTER ABSTRACTS

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

Trial in Progress: Treatment of Newly-Diagnosed Follicular Lymphoma with Celmod BMS-986369, Rituximab +/- Nivolumab: An Umbrella Phase II Investigator-Initiated Study

Geoff Chong, MD[1], *Jodie B Palmer, PhD*[2,3], *Allison A Barraclough, BSc,FRACP,FRCPA,MBBS*[4], *Leonid Churilov, PhD*[5], *Colm Keane, MD*[6], *Sze Ting Lee, MBBS, FRACP, FAANMS, PhD*[7], *Denise Lee, MBBS, FRCPA, FRACP*[8], *Sumita Ratnasingam, MDFRACP,FRCPA*[9], *Charmaine Smith*[10], *Eliza A Hawkes, MD*[11,12]

[1] Grampians Health, Ballarat, Australia
[2] Olivia Newton-John Cancer Research Institute, Heidelberg, Australia
[3] School of Cancer Medicine, La Trobe University, Heidelberg, Australia
[4] Haematology Department Fiona Stanley Hospital Murdoch, wa, Australia
[5] University of Melbourne, Parkville, AUS
[6] Frazer Institute, Translational Research Institute, University of Queensland, Brisbane, Australia
[7] Dept Molecular Imaging and Therapeutics, Austin Health, Heidelberg, Australia
[8] Eastern Health Clinical School, Monash University, Eastern Health, Box Hill, Australia
[9] Barwon Health, Geelong, AUS
[10] Austin Health, Heidelberg, AUS
[11] Department of Clinical Haematology and Medical Oncology, Austin Health, Heidelberg, Australia
[12] Dept of Haematology & Medical Oncology and Olivia Newton John Cancer Research Institute, Austin Health, Melbourne, Australia

Background: Follicular lymphoma (FL) outcomes are influenced by tumour microenvironment composition and manipulation. As patients (pts) with FL are predominantely aged over 65 and may require treatment multiple times over their disease course, novel regimens which maintain or enhance efficacy and minimise toxicity are highly desirable.
We have previously reported favourable efficacy and safety of nivolumab plus rituximab as a 1 st line treatment in advanced-stage, grade 1-3A treatment naïve FL, (ORR 92%; CR 54%; toxicity grade 3 or higher in 41%) in an investigator-led trial. [1-3] Oral cereblon-modulating (CELMoD) compounds have shown substantial efficacy alone or in combination with rituximab in both treatment naive and relapsed/refractory FL. [4,5] CELMoDs co-opt cereblon to promote degradation of key transcription factors in cell development and homeostasis, including Ikaros and Aiolos, which are upregulated in FL. [6] Additionally, they act as immunomodulatory agents and augment immune host response. The novel CELMoD, BMS-986369 (golcadomide), demonstrated enhanced antiproliferative and apoptotic activity in pre-clinical studies, with ORR of up to 75% following monotherapy doses of 0.4mg or higher in heavily pre-treated FL pts. [7-10] Our follow-on study ('TOP-FLOR'; NCT05788081) builds on these findings and potential immunomodulatory synergy to explore the efficacy and safety of BMS-986369 with rituximab +/-nivolumab in treatment-naïve advanced stage FL pts.
Study Design and methods: This is an open label multicentre umbrella Bayesian Optimal randomised Phase II trial. The study will randomise up to 40 eligible pts 1:1 to receive rituximab, BMS986369 +/- nivolumab (20 per arm) from 5 Australian sites. Eligibility includes pts aged >18 years, with previously-untreated, stage II-IV, grade 1-3A FL with performance status of 0-1 who require systemic therapy. Treatment consists of 8 cycles (28 days each) of BMS-986369 0.4 mg po daily on days 1- 14 plus rituximab 375 mg/m2 IV day 1 in Arm A; BMS-986369, rituximab as above plus nivolumab 480mg IV day 1 in Arm B. All pts in partial or complete response at end of induction receive 12-weekly rituximab maintenance (8 doses).
The primary endpoint will be CR rate in the absence of prohibitive toxicity in accordance with CTCAE V5.0 after eight cycles of rituximab, BMS-986369 +/-nivolumab. Secondary endpoints include: Overall toxicity, response rate (according to modified Lugano criteria), time to treatment failure, progression-free survival and overall survival. Exploratory endpoints include: pt reported outcomes as measured by EORTC-QLQ-c30 and FACT-Lym, PET radiomics and tissue, blood and stool immune and genomic biomarkers.

Study assessments include: PET/CT, biomarker blood collection and pt reported outcome measures performed at baseline, post cycle 2, 5 and 8, then 6 monthly on maintenance therapy. Response assessment according to modified Lugano criteria. Safety assessments prior to each cycle until 28 days after the final study drug is administered using CTCAEv5.0. Interim assessment of the primary endpoint will be conducted for 11 pts in each arm, arms will be closed for futility if fewer than 7 pts achieve the primary endpoint. Treatment arms will not be formally compared. Survival probabilities will be reported using Kaplan-Meier analysis.

Status: This trial received IRB approval on 14 July 2023 (HREC/88597/Austin-2023) at Austin Health, Heidelberg, Australia.

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Disclosures Chong: *Bristol-Myers Squibb:* Consultancy, Research Funding; *Regeneron:* Research Funding; *Merck Serono:* Research Funding; *Astra Zeneca:* Research Funding; *HutchMed:* Research Funding; *Incyte:* Research Funding; *Morphosys:* Research Funding; *Bayer:* Research Funding; *Isofol:* Research Funding; *Servier:* Research Funding; *Dizal Pharma:* Research Funding. **Barraclough:** *Roche:* Honoraria; *Gilead:* Consultancy, Honoraria. **Keane:** *Roche:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *Takeda:* Speakers Bureau; *MSD:* Membership on an entity's Board of Directors or advisory committees, Research Funding; *Janssen:* Consultancy; *Gilead:* Membership on an entity's Board of Directors or advisory committees; *Karyopharm:* Consultancy; *Beigene:* Consultancy; *AstraZeneca:* Speakers Bureau; *Bristol Myers Squibb:* Research Funding. **Hawkes:** *Novartis:* Membership on an entity's Board of Directors or advisory committees, Other; *Janssen:* Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *Merck Sharpe & Dohme:* Membership on an entity's Board of Directors or advisory committees; *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; *Merck KgA:* Research Funding; *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; *Antengene:* Membership on an entity's Board of Directors or advisory committees; *Beigene:* Other; *Specialised Therapeutics:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Regeneron:* Speakers Bureau.

OffLabel Disclosure: BMS-986369 is a CELMoD which is not an approved drug, nor approved for this indication.

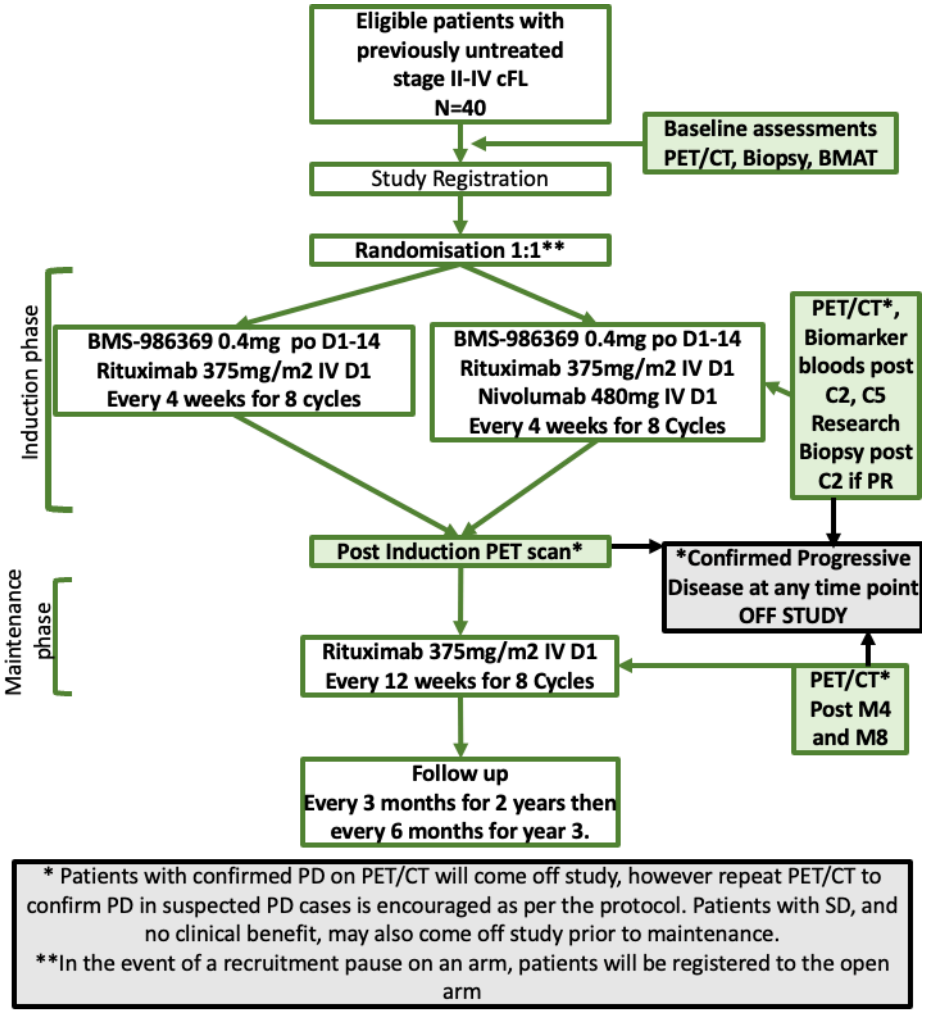

Figure 1 TOP-FLOR Study Schema and Treatment Schedule

Figure 1

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