ELSEVIER

Blood 142 (2023) 3034–3036

The 65th ASH Annual Meeting Abstracts

POSTER ABSTRACTS

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

Phase II Trial of Ibrutinib in Previously Untreated High-Risk Smoldering Mantle Cell Lymphoma

Charles Gaulin, MBBS[1], Preetesh Jain, MDMBBS,PhDDM[2], Ranjit Nair, MD[1,3], Swami P. Iyer, MD[2], Hun Ju Lee, MD[1], Luis Fayad, MD[4], Lei Feng, MS[5], Yang Liu, PhD[1], Holly A Hill, MS[6], Yijing Li, BS, MS[1], Chi Young Ok, MD[7], Rashmi Kanagal-Shamanna, MD[8], Onyeka Oriabure, MSN, RN, NP[6], Wendy Chen, BS,MPAS,MS[6], Asiya Siddiqui, MS[2], Guofan Xu, MBBS, PhD[9], Anita Deswal, MD MPH, MBBS[10], Cezar Iliescu, MD[11], Maria Badillo[12], Shaoying Li, MD[13], Michelle Ky[2], Michelle Avellaneda[2], Guilin Tang, MD PhD[7], Francisco Vega, MDPhD[14], Christopher R. Flowers, MD MS[1], Michael L. Wang, MD[2]

[1] Department of Lymphoma and Myeloma, The University of Texas MD Anderson Cancer Center, Houston, TX
[2] Lymphoma and Myeloma, The University of Texas MD Anderson Cancer Center, Houston, TX
[3] Department of Lymphoma and Myeloma, The University of Texas MD Anderson Cancer Center, Pearland, TX
[4] Lymphoma/Myeloma, M.D. Anderson Cancer Center, Houston, TX
[5] Biostatistics, UT MD Anderson Cancer Center, Houston, TX
[6] Departments of Lymphoma and Myeloma, The University of Texas MD Anderson Cancer Center, Houston, TX
[7] Hematopathology, The University of Texas MD Anderson Cancer Center, Houston, TX
[8] Department of Hematopathology, The University of Texas M D Anderson Cancer Center, Houston, TX
[9] Cardiology, University of Texas MD Anderson Cancer Center, Houston, TX
[10] Geriatrics, MD Anderson Cancer Center, Houston, TX
[11] Cardiology, The University of Texas MD Anderson Cancer Center, houston, TX
[12] Lymphoma/ Myeloma, The University of Texas MD Anderson Cancer Center, Houston, TX
[13] The University of Texas MD Anderson Cancer Center, Houston, TX
[14] Department of Hematopathology, MD Anderson Cancer Center , Houston, TX

Background: Mantle cell lymphoma (MCL) patients usually require immediate therapy, however about 20% of newly diagnosed MCL patients can be initially observed. A subgroup of patients who are suitable for initial observation but exhibit high-risk features are of particular concern as they have a propensity to progress. We consider these patients as high-risk smoldering MCL (defined below). Generally, these patients are observed without systemic therapy for 18-24 months. We investigated the impact of single-agent ibrutinib on time to progression for these patients who would otherwise be observed.
Methods: This is a single center, single arm, investigator-initiated phase 2 clinical trial (NCT03282396). High-risk smoldering MCL included one or more of the following criteria: non-blastoid/pleomorphic variant, Ki-67 of 15-30%, white blood cell count of 15-30 x 10^9/L, lymph nodes ≤5 cm, *TP53* mutated or wild type, del17p, MYC positive, complex karyotype, presence of KMT2D, BIRC3, or ≥1 other somatic mutations, and were asymptomatic without any clinical indication to start systemic therapy. Major exclusion criteria included significant disease-related symptoms, blastoid/pleomorphic variants, Ki-67 >30%, bulky tumors >5 cm. Patients received ibrutinib 560 mg P.O. daily in 28-day cycles and continued until progression, transformation, drug intolerance, or up to 5 years. The primary endpoint was progression-free survival (PFS). Secondary endpoints were safety, response rate, and duration of response (DOR). Response was measured using the Lugano criteria. It is expected that the current trial will achieve a median PFS time of about 18 months, which would be an improvement over PFS reported on high-risk patients under a watch and wait approach. The median follow-up time was 23.4 months.
Results: Twenty patients were enrolled (Table 1). The median age was 60.5 years (range 38-79). Most were male (n=15/20). At baseline, 13 patients (65%) had bone marrow involvement and 15 patients (75%) had gastrointestinal tract involvement. Seven patients (35%) had *TP53* alterations. One patient was not evaluable for response due cessation of therapy after less than 1 cycle due to new onset atrial fibrillation. Among 19 evaluable patients, the best overall response rate was 94.7% (n=18/19). Of those who had a positive PET at baseline and were evaluable for PET response, 92.9% (n=13/14) achieved a PET complete response (CR). Of those with bone marrow involvement at baseline, 30.7% (n=4/13) achieved CR by flow cytometry. Of those with baseline gastrointestinal tract involvement, 33.3% (n=5/15) achieved histologically confirmed CR. The median number

of cycles received was 16 (range 0-32). The median PFS and DOR were not reached. Seven patients discontinued therapy: atrial fibrillation (n=3), progressive disease (n=1), infection (n=1), lung cancer (n=1). The most frequent grade 3 toxicities were diarrhea (n=2, 10%), atrial fibrillation (n=1, 5%), infection (n=1, 5%), mucositis (n=1, 5%), and syncope (n=1, 5%). No grade 4 toxicities occurred. No deaths on study occurred.
Conclusions: Ibrutinib demonstrated significant efficacy with manageable toxicities in previously untreated patients with high-risk smoldering MCL.

Disclosures Gaulin: *ADC Therapeutics:* Consultancy; *DeciBio:* Consultancy. **Jain:** *AstraZeneca:* Consultancy, Honoraria. **Iyer:** *Yingli:* Consultancy, Research Funding; *Drenbio:* Research Funding; *Salarius:* Consultancy; *Pfizer:* Research Funding; *Ono:* Research Funding; *Astra Zeneca:* Research Funding; *Legend:* Research Funding; *Acrotech:* Consultancy, Research Funding; *Innate:* Research Funding; *CRISPR:* Consultancy, Research Funding; *Merck:* Research Funding; *Seagen:* Consultancy, Research Funding; *CuraBio:* Speakers Bureau; *American Society of Hematology:* Speakers Bureau; *American Society of Transplant and Cellular Therapy:* Speakers Bureau. **Lee:** *Takeda:* Research Funding; *Korean Society of Cardiology:* Honoraria; *Seagen Inc.:* Research Funding; *Olson Research:* Honoraria; *Oncternal Therapeutics:* Research Funding; *Pharmacyclics:* Research Funding; *Janssen:* Honoraria; *Guidepoint:* Honoraria; *Deloitte:* Honoraria; *Curio Sciences:* Honoraria; *Century Therapeutics:* Consultancy; *Celgene:* Research Funding; *Cancer Experts:* Honoraria; *Bristol-Myers Squibb:* Research Funding; *Aptitude Health:* Honoraria. **Vega:** *Geron:* Research Funding; *Allogene:* Research Funding. **Flowers:** *Allogene:* Research Funding; *Iovance:* Research Funding; *Denovo Biopharma:* Consultancy; *Takeda:* Research Funding; *Sanofi:* Research Funding; *Ziopharm:* Research Funding; *Cellectis:* Research Funding; *Karyopharm:* Consultancy; *Cancer Prevention and Research Institute of Texas:* Research Funding; *Bayer:* Consultancy, Research Funding; *Jannsen Pharmaceuticals:* Research Funding; *N-Power Medicine:* Consultancy, Current holder of *stock options* in a privately-held company; *Amgen:* Research Funding; *Guardant:* Research Funding; *Morphosys:* Research Funding; *Adaptimmune:* Research Funding; *Nektar:* Research Funding; *Kite:* Research Funding; *Beigene:* Consultancy; *Eastern Cooperative Oncology Group:* Research Funding; *Burroghs Wellcome Fund:* Research Funding; *Abbvie:* Consultancy, Research Funding; *Foresight Diagnostics:* Consultancy, Current holder of *stock options* in a privately-held company; *Celgene:* Consultancy, Research Funding; *Genmab:* Consultancy; *Genentech Roche:* Consultancy, Research Funding; *Gilead:* Consultancy, Research Funding; *Pharmacyclics:* Research Funding; *Pharmacyclics Jansen:* Consultancy; *SeaGen:* Consultancy; *Spectrum:* Consultancy; *4D:* Research Funding; *Pfizer:* Research Funding; *Novartis:* Research Funding; *TG Therapeutics:* Research Funding; *Xencor:* Research Funding; *V Foundation:* Research Funding; *National Cancer Institute:* Research Funding; *Acerta:* Research Funding; *CPRIT Scholar in Cancer Research:* Research Funding. **Wang:** *Loxo Oncology:* Research Funding; *Juno Therapeutics:* Research Funding; *Genentech:* Research Funding; *Celgene:* Other: Travel, Research Funding; *WebMD:* Honoraria; *Oncology Specialty Group:* Honoraria; *Nurix:* Honoraria; *NIH:* Honoraria; *Moffit Cancer Center:* Honoraria; *MJH Life Sciences:* Honoraria; *MD Education:* Honoraria; *Meeting Minds Experts:* Honoraria; *Medscape:* Honoraria; *IDEOlogy Health:* Honoraria; *i3Health:* Honoraria; *Genmab:* Honoraria, Research Funding; *Eastern Virginia Medical School:* Honoraria; *Dava Oncology:* Honoraria, Other: Travel; *CAHON:* Honoraria; *Bantam Pharmaceutical:* Honoraria; *VelosBio:* Consultancy, Research Funding; *Pharmacyclics:* Consultancy, Honoraria, Research Funding; *Pepromene Bio:* Consultancy; *Parexel:* Consultancy; *Oncternal:* Consultancy, Research Funding; *Milken Institute:* Consultancy; *Miltenyi Biomedicine:* Consultancy; *Merck:* Consultancy, Honoraria; *Eli Lilly and Company:* Consultancy, Research Funding; *Leukemia & Lymphoma Society:* Consultancy, Honoraria; *Kite Pharma:* Consultancy, Honoraria, Other: Travel, Research Funding; *Janssen:* Consultancy, Honoraria, Research Funding; *InnoCare:* Consultancy; *Genentech:* Consultancy; *DTRM Biopharma (Cayman) Limited:* Consultancy; *Deciphera:* Consultancy; *Bristol Myers Squibb:* Consultancy, Honoraria; *BioInvent:* Consultancy, Honoraria, Research Funding; *BeiGene:* Consultancy, Honoraria, Research Funding; *Be Biopharma:* Consultancy; *AstraZeneca:* Consultancy, Honoraria, Other: Travel, Research Funding; *Amphista Therapeutics Limited:* Consultancy; *ADC Therapeutics America:* Consultancy; *Acerta Pharma:* Consultancy, Honoraria, Research Funding; *AbbVie:* Consultancy, Honoraria; *OncLive:* Honoraria; *Studio ER Congressi:* Honoraria; *Physicians Education Resources (PER):* Honoraria, Other: Travel; *Scripps:* Honoraria; *Practice Point Communications (PPC):* Honoraria; *Molecular Templates:* Research Funding; *Vincerx:* Research Funding.

OffLabel Disclosure: Ibrutinib in previously untreated smoldering mantle cell lymphoma

Table 1. Patient Characteristics and Outcomes	
	All Patients (n=20)
Median Age (years, range)	60.5 (38-79)
Gender (male)	15
Disease Characteristics at Baseline	
PET Positive	70% (n=14/20)
Bone Marrow Involvement	65% (n=13/20)
Gastrointestinal Tract Involvement	75% (n=15/20)
High-Risk Features	
Ki-67 15-30%	55% (n=11/20)
TP53 Alteration	35% (n=7/20)
Multiple Somatic Mutations	35% (n=7/20)
Complex Karyotype	15% (n=3/20)
MYC Positive	10% (n=2/20)
WBC count 15-30 x 10^9/L	25% (n=5/20)
LN diameter 3-5 cm	15% (n=3/20)
Best Response	**Evaluable Patients (n=19)**
ORR	94.7% (n=18/19)
PET CR	92.9% (n=13/14)
Bone Marrow CR	30.7% (n=4/13)
Gastrointestinal Tract CR	33.3% (n=5/15)
PR	52.6% (n=10/19)
SD	5.3% (n=1/19)
Median Follow-up (months, 95% CI)	23.4 (19.2-27.5)
Median PFS	Not Reached
Median DOR	Not Reached

Legend: WBC=white blood cell; LN=lymph node; ORR=overall response rate; PET=positron emission tomography; CR=complete response; CR*=complete response with histologically confirmed clearance of bone marrow and gastrointestinal tract; PR=partial response; SD=stable disease; CI=confidence interval; PFS=progression-free survival; DOR=duration of response

Figure 1

https://doi.org/10.1182/blood-2023-187903