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ASH Abstracts
2020

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2020 ASH Annual Meeting Abstracts
Blood 2020

Selected abstracts
Abstracts #3152, #3140, #3146, #2223, #1317

62nd ASH Annual Meeting and Exposition
December 5-8, 2020

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Abstract 3152

Comparison between Time-Limited, Venetoclax-Based and Continuous Bruton Thyrosine Kinase Inhibitors-Based Therapy in the Upfront Treatment of Chronic Lymphocytic Leukemia (CLL): a Systematic Review and Network Meta-Analysis

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Background: Targeted agents (TAs) have shown impressive activity in the upfront treatment of chronic lymphocytic leukemia (CLL). However, TAs have rarely been compared in head-to-head clinical trials. With this background, a systematic literature review and network meta-analysis (NMA) was performed to estimate the relative efficacy of TAs approved by the FDA and/or EMA for upfront therapy of CLL (i.e., ibrutinib, acalabrutinib, and venetoclax).

Methods: A systematic search of MEDLINE, EMBASE, BioSciences Information Service, and the Cochrane Library databases was conducted. Eligible studies consisted of randomized controlled trials (RCTs) assessing the efficacy or safety of TAs in previously untreated CLL patients. Outcomes considered were hazard ratios for progression-free survival (PFS), odds ratios for overall response rate (ORR) and adverse event rates. A given treatment was considered more effective than another one when a 95% upper confidence interval (CI) for relative risk (RR) did not cross the value 1.0 (equivalent to a Bayesian probability for this pairwise comparison p≥97.5%).

Results: Among relevant RCTs, 6 met criteria of low risk for bias according to the Cochrane Handbook for Systematic Reviews of Interventions and were selected for analysis. Three studies were excluded because they lacked a common comparator arm (i.e., RESONATE2, ALLIANCE, and ECOG-ACRIN). Three trials were suitable for the base-case network analysis (i.e., ILLUMINATE, ELEVATE-TN, and CLL14). In aggregate, these trials included 1336 patients and evaluated the combination of ibrutinib-obinutuzumab (IO) (ILLUMINATE trial; n=113), venetoclax-obinutuzumab (VO) (CLL14 trial; n=216) and acalabrutinib (A) single agent (ELEVATE-TN trial; n=179). Chlorambucil-obinutuzumab (CO) was the control arm across these studies (n=504). Since results of A plus obinutuzumab (AO) (n=179) in the ELEVATE-TN trial were based on a post-hoc analysis they were not included in the NMA.

In terms of PFS, fixed-effect analyses comparing VO to IO (RR 1.52[0.82–2.81]), A to IO (RR 0.87 [0.47–1.61]) and A to VO (RR 0.57[0.32–1.03]) revealed that the upper limit of 95% CI for RR did exceed the 1.0 value (Fig 1). This implies a lack of significant difference in PFS for IO, VO, and acalabrutinib. Similarly, no differences with respect to ORR were found in the indirect comparison of different TAs: VO *vs.* IO (RR 0.98 [0.61–1.59]), A *vs.* IO (RR 0.90[0.55–1.48]) and A *vs.* VO (RR 0.92[0.60–1.40]). The analysis of treatment side effects was performed comparing in aggregate all adverse events (AEs). No differences in the frequency of AEs was observed across different TAs: VO *vs.* IO (RR 1.00 [0.63–1.58]), A *vs.* IO (RR 1.01[0.62–1.63]) and A *vs.* VO (RR 1.01[0.68–1.52]). The same applied when the analysis was restricted to events with grade 3–4 toxicity: VO *vs.* IO (RR 1.05[0.64–1.73]), A *vs.* IO (RR 0.73[0.43–1.24]) and A *vs.* VO (RR 0.69[0.44–1.09]).

Conclusions: This systematic review and network meta-analysis did not identify significant differences in PFS between BTKi-and time-limited venetoclax-based treatments in CLL upfront therapy. Further trials are needed to ascertain the pros and cons of different targeted treatments. Meanwhile, treatment selection in routine clinical practice should be based on drugs' safety, cost, availability, and treatment objectives.

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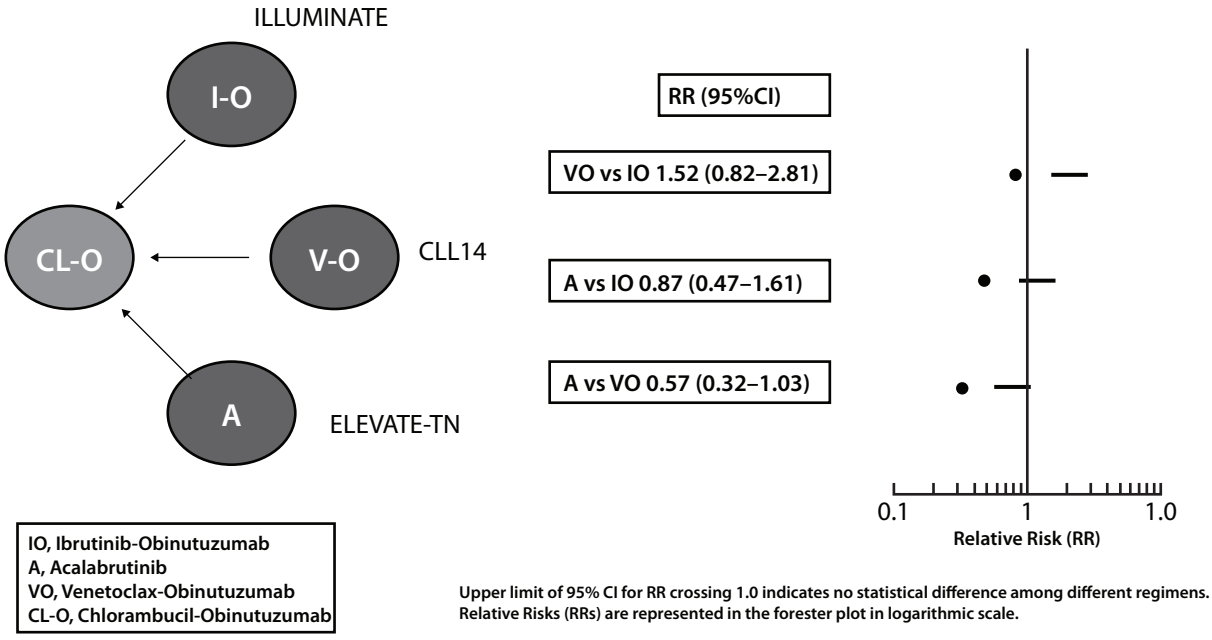
Figure.



Upper limit of 95% CI for RR crossing 1.0 indicates no statistical difference among different regimens. Relative Risks (RRs) are represented in the forester plot in logarithmic scale.

Disclosures: Molica: *Gilead:* 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; *Roche:* Membership on an entity's Board of Directors or advisory committees; *Abbvie:* Membership on an entity's Board of Directors or advisory committees, Speakers Bureau.

Abstract 3140

Acalabrutinib Vs Idelalisib Plus Rituximab or Bendamustine Plus Rituximab in Relapsed/Refractory Chronic Lymphocytic Leukemia: Ascend Final Results

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Background: Acalabrutinib (acala) is a next-generation, highly selective, covalent Bruton tyrosine kinase inhibitor approved for patients with chronic lymphocytic leukemia (CLL) including those with relapsed/refractory (R/R) CLL. The efficacy and safety of acala alone versus idelalisib (Id) plus rituximab (R) (IdR) or bendamustine (B) plus R (BR) were shown in patients with R/R CLL in a preplanned interim analysis of ASCEND; final results are reported herein.

Methods: In this randomized, multicenter, phase 3, open-label study (NCT02970318), patients with R/R CLL were randomized 1:1 to receive oral (PO) acala 100 mg twice daily (BID) or investigator's (INV) choice of IdR (Id: 150 mg PO BID until progression or toxicity; R: 375 x1 then 500 mg/m^2 intravenously [IV] for 8 total infusions) or BR (B: 70 mg/m^2 IV and R: 375 x1 then 500 mg/m^2 IV for 6 total cycles) until progression or toxicity. Progression-free survival (PFS), overall survival (OS), overall response rate (ORR), and safety were assessed.

Results: 310 patients (acala, n=155; IdR, n=119; BR, n=36) were enrolled (median age: 67 y; del(17p) 16%, del(11q) 27%, Rai stage 3/4 42%). At a median follow-up of 22.0 m, acala significantly prolonged INV-assessed PFS vs IdR/BR (median: not reached vs 16.8 m; hazard ratio: 0.27, P<0.0001); 18-m PFS rates were 82% for acala and 48% for IdR/BR. 18-m OS rate was 88% for both treatment regimens. ORR was 80% with acala vs 84% with IdR/BR (ORR + partial response with lymphocytosis: 92% vs 88%, respectively). Common adverse events (AEs) are listed in the **Table**. AEs led to drug discontinuation in 16% of acala, 56% of IdR, and 17% of BR patients. AEs of interest included atrial fibrillation (acala 6%, IdR/BR 3%), major hemorrhage (all grade; acala 3%, IdR/BR 3%), grade ≥3 infections (acala 20%, IdR/BR 25%), and second primary malignancies excluding non-melanoma skin cancer (acala 5%, IdR/BR 2%).

Conclusions: Final ASCEND results with additional follow-up confirm earlier findings and support the favorable efficacy and safety of acala compared with standard-of-care regimens in patients with R/R CLL.

Table.

	Acala		IdR		BR	
	Any Grade	**Grade ≥3**	**Any Grade**	**Grade ≥3**	**Any Grade**	**Grade ≥3**
Common AEs[a], n(%)						
Headache	34 (22)	1 (1)	7 (6)	0	0	0
Neutropenia	33 (21)	26 (17)	54 (46)	47 (40)	12 (34)	11 (31)
Diarrhea	30 (20)	3 (2)	58 (49)	29 (25)	5 (14)	0
Upper respiratory tract infection	30 (20)	3 (2)	19 (16)	4 (3)	4 (11)	1 (3)
Cough	25 (16)	0	18 (15)	1 (1)	2 (6)	0
Anemia	24 (16)	19 (12)	11 (9)	8 (7)	4 (11)	3 (9)
Pyrexia	21 (14)	1 (1)	22 (19)	8 (7)	6 (17)	1 (3)
Fatigue	17 (11)	2 (1)	10 (9)	1 (1)	8 (23)	1 (3)
Nausea	11 (7)	0	16 (14)	1 (1)	7 (20)	0
Infusion-related reaction	0	0	9 (8)	2 (2)	8 (23)	1 (3)

[a]Any grade in ≥15% of patients.

Disclosures: Ghia: *Novartis:* Research Funding; *ArQule:* Consultancy, Honoraria; *Acerta/AstraZeneca:* Consultancy, Honoraria; *Adaptive, Dynamo:* Consultancy, Honoraria; *Gilead:* Consultancy, Honoraria, Research Funding; *BeiGene:* Consultancy, Honoraria; *Janssen:* Consultancy, Honoraria, Other: TRAVEL, ACCOMMODATIONS, EXPENSES (paid by any for-profit health care company), Research Funding; *Celgene/Juno:* Consultancy, Honoraria; *Lilly:* Consultancy, Honoraria; *MEI:* Consultancy, Honoraria; *Sunesis:* Consultancy, Honoraria, Research Funding; *AbbVie:* Consultancy, Honoraria, Other: TRAVEL, ACCOMMODATIONS, EXPENSES (paid by any for-profit health care company), Research Funding. **Pluta:** *Janssen-Cilag, Kartos Therapeutics, Iqvia, Roche, Acerta Pharma, Pharmacyclics, BeiGene, Takeda:* Research Funding; *Celgene, Servier, Takeda, Novartis:* Honoraria; *Celgene:* Other: Travel, Accommodations, Expenses. **Lysak:** *Abbvie, Novartis, Roche, Janssen-Cilag:* Consultancy. **Kozak:** *Amgen, Novartis, Abbvie, Gilead Sciences:* Consultancy; *Abbvie, Tak:* Other: Travel, Accommodations, Expenses. **Šimkovič:** *Acerta Pharma:* Consultancy; *Gilead Sciences:* Consultancy, Other: Travel, Accommodations, Expenses; *Janssen-Cilag:* Consultancy, Honoraria, Other: TRAVEL, ACCOMMODATIONS, EXPENSES (paid by any for-profit health care company), Speakers Bureau; *University Hospital Hradec Kralove:* Current Employment; *AbbVie:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Other: TRAVEL, ACCOMMODATIONS, EXPENSES (paid by any for-profit health care company), Speakers Bureau. **Kryachok:** *Takeda, Roche, Abbvie, MSD Oncology:* Other: Travel, Accommodations, Expenses; *Janssen Oncology, Bayer, Karyopharm Therapeutics, MSD Oncology, Acerta Pharma, Abbvie, Debiopharm Group:* Research Funding; *Takeda, Janssen Oncology:* Consultancy. **Illés:** *Takeda, Seattle Genetics:* Research Funding; *Novartis, Janssen, Pfizer, Roche;:* Other: Travel, Accommodations, Expenses; *Celgene, Janssen, Novartis, Roche, Takeda:* Consultancy; *Janssen, Celgene, Takeda, Novartis Pharma SAS, Pfizer Pharmaceuticals Israel, Roche;:* Consultancy, Honoraria. **de la Serna:** *Abbvie, Janssen:* Speakers Bureau; *Abbvie, AstraZeneca:* Other: Travel, Accommodations, Expenses; *Gilead, AstraZeneca, Abbvie, Janssen, Sandoz, F. Hoffmann-La Roche:* Consultancy; *Abbvie, Pharmacyclics, Novartis, Janssen, Acerta, AstraZeneca, BioGene, UCB, Sandoz:* Honoraria; *F. Hoffmann-La Roche, Abbvie, Pharmacyclics, Gilead, GlaxoSmithKline, Novartis, Janssen, Roche, Acerta, AstraZeneca, BioGene, UCB:* Research Funding. **Campbell:** *Amgen, Novartis, Roche, Janssen, Celgene (BMS):* Research Funding; *AstraZeneca, Janssen, Roche, Amgen, CSL Behring, Novartis:* Consultancy. **Musuraca:** *AstraZeneca, Debiopharm Group, Janssen, Gilead Sciences:* Consultancy; *TG Therapeutics, Acerta Pharma, AstraZeneca, Janssen, Bayer, Debiopharm Group, Epizyme, Merck, MorphoSys, MEI Pharma, Celerion, Roche, Servier, BeiGene:* Research Funding. **Jacob:** *AstraZeneca:* Consultancy, Honoraria, Research Funding; *AstraZeneca, GlaxoSmithKline, Horizon Discovery, Oxford Biomedica, Midlands Haematology Services:* Current equity holder in publicly-traded company. **Avery:** *AstraZeneca:* Consultancy, Other: Travel, Accommodations, Expenses; *Lilly:* Research Funding. **Wang:** *Acerta Pharma LLC:* Current Employment; *Global Blood Therapeutics.:* Consultancy. **Patel:** *AstraZeneca:* Current Employment, Current equity holder in publicly-traded company. **Jurczak:** *Jagiellonian University:* Ended employment in the past 24 months, Research Funding; *Janssen, MeiPharma, Merck, Pharmacyclics, Roche, Takeda, TG Therapeutics:* Research Funding; *Maria Sklodowska-Curie National Research Institute of Oncology:* Consultancy, Current Employment.

Abstract 3146

Pooled Analysis of Cardiovascular Events from Clinical Trials Evaluating Acalabrutinib Monotherapy in Patients with Chronic Lymphocytic Leukemia (CLL)

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Background: Bruton tyrosine kinase (BTK) inhibitors are effective treatments for B-cell malignancies, but an increased incidence of cardiovascular (CV) toxicities has been observed with ibrutinib. Acalabrutinib (acala) is a next-generation, potent, highly selective, covalent BTK inhibitor approved for chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma and mantle cell lymphoma. The objective of this analysis was to characterize CV adverse events (AEs) in patients (pts) with CLL who received acala monotherapy.

Methods: Data from pts with CLL in 4 studies (ACE-CL-001 [NCT02029443]; ACE-CL-007 [ELEVATE-TN, NCT02475681]; ACE-CL-309 [ASCEND, NCT02970318]; 15-H-0016 [NCT02337829]) were pooled. Cutoff dates ranged from December 2018 to February 2019. Pts who received ≥1 dose of acala monotherapy were included. For pts who crossed over from control arms to acala, only AEs recorded after crossover were included. Acala was given orally at total daily doses of 100 mg to 400 mg, later switched to 100 mg twice daily, and continued until disease progression (PD) or toxicity. Cardiac AEs and hypertension (htn) were examined.

Results: 762 pts were included (treatment-naïve: n=352 [46%]; relapsed/refractory: n=410 [54%]; median age: 67 years [range: 32–89]; Eastern Cooperative Oncology Group performance status ≤1: 93%; median acala exposure: 24.9 mo [range: 0–58.5]; median follow-up: 25.9 mo [range: 0–58.5]). A total of 199 cardiac AEs of any grade (irrespective of treatment relationship) were reported in 129 pts (17%). Cardiac AEs led to treatment discontinuation in 7 pts (0.9%). The most frequent cardiac AEs reported in ≥2% of pts were atrial fibrillation (afib: n=34; 4%; afib/flutter: n=38; 5%), palpitations (n=23; 3%), and tachycardia (n=17; 2%). The median time to afib/flutter onset was 521 days (range: 8–1280). Overall, 91% (117/129) of pts with vs 79% (503/633) without cardiac AEs had ≥1 CV risk factor before acala initiation. The most prevalent CV risk factors (≥20%) among the 129 pts with cardiac AEs were htn (n=86; 67%), hyperlipidemia (n=38; 29%), and arrhythmias (n=29; 22% [afib: n=16; 12%]). Htn AEs were reported in 9% (67/762) of pts, among whom 46 (69%) had pre-existing htn and 18 (27%) had htn risk factors. The median time to htn onset was 197 days (range: 2–1345).

Thirty-seven pts (4%) had 51 grade ≥3 cardiac AEs (grade 3: n=37; grade 4: n=12; grade 5: n=2). Grade ≥3 cardiac AEs of interest included afib (n=10; 1.3%), complete atrioventricular (AV) block (n=2; 0.3%), acute coronary syndrome (n=1; 0.1%), atrial flutter (n=1; 0.1%), second degree AV block (n=1; 0.1%), and ventricular fibrillation (n=1; 0.1%). Two patients experienced grade 5 AEs (cardiac failure congestive [n=1], acute myocardial infarction [n=1]). Among the 37 pts with grade ≥3 AEs, 18 (49%) were continuing acala at data cutoff; 6 (16%) had discontinued due to the grade ≥3 cardiac AEs, 4 (11%) to other AEs, 5 (14%) to PD, 3 (8%) to death, and 1 (3%) to other reasons. Among the 51 grade ≥3 cardiac AEs, 16 (31%) led to dose delay and 36 (71%) were managed with concomitant medications. Most events (43/51 [84%]) resolved (dose delay: n=15; drug withdrawal: n=4; no dose change: n=24).

Cardiac AEs occurring in the first 6 mo on acala were assessed based on a predominance of AEs (afib) during this time period with ibrutinib (Brown JR, et al, *Haematologica.* 2017;102:1796). Overall, 48% of pts with any-grade cardiac AEs experienced them in the first 6 mo on acala. Thirteen grade ≥3 cardiac AEs (25% of total) were observed in 9 pts in the first 6 mo (**Table**); all but 1 AE (grade 4 cardiac tamponade resulting in hospitalization) were managed with concomitant medications. Two of the 13 AEs resulted in treatment discontinuation (**Table**).

Conclusions: At a median exposure of 24.9 mo, cardiac AEs occurred infrequently in pts with CLL treated with acala monotherapy; only 0.9% discontinued treatment due to cardiac AEs. Among grade ≥3 cardiac AEs, 25% were reported during the first 6 mo on treatment. Most pts with cardiac AEs had pre-existing risk factors that may have contributed to their development. The incidence of afib with acala (4%) was comparable to that of the general CLL population (6.1%; Shanafelt TD, et al. *Leuk Lymphoma.* 2017;58:1630). These data suggest a low risk of cardiac AEs with acala treatment in pts with CLL. The safety of acala vs ibrutinib in pts with high-risk CLL will be investigated in the phase 3, randomized ACE-CL-006 trial (NCT02477696).

Table. Grade ≥ cardiac events occurring within the first 6 mo an acalabrutinib treatment

Patient number	Event	Grade	Dose modification/ treatment discontinuation	Outcome
1	Coronary artery stenosis	4	Dose delay	Resolved
2	Cardiac tamponade	4	Dose not changed	Resolved
3	Cardiac failure	4	Dose not changed	Ongoing
4	Acute myocardial infarction Atrial fibrillation	3 3	Dose delay Dose delay	Resolved Resolved
5	Acute coronary syndrome Angina unstable	3 3	Dose delay Dose not changed	Resolved Resolved
6	Atrial fibrillation	3	Dose not changed	Resolved
7	Atrial fibrillation Cardiac failure congestive	3 3	Dose not changed Treatment discontinuation	Resolved Resolved
8	Cardiac failure	3	Treatment discontinuation	Resolved
9	Cardiac failure congestive Pericarditis constrictive	3 3	Dose not changed Dose delay	Resolved Resolved

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Abstract 2223

Evaluation of the Incidence and Risk Factors Associated with Major Cardiovascular Events in Patients Receiving Acalabrutinib Therapy

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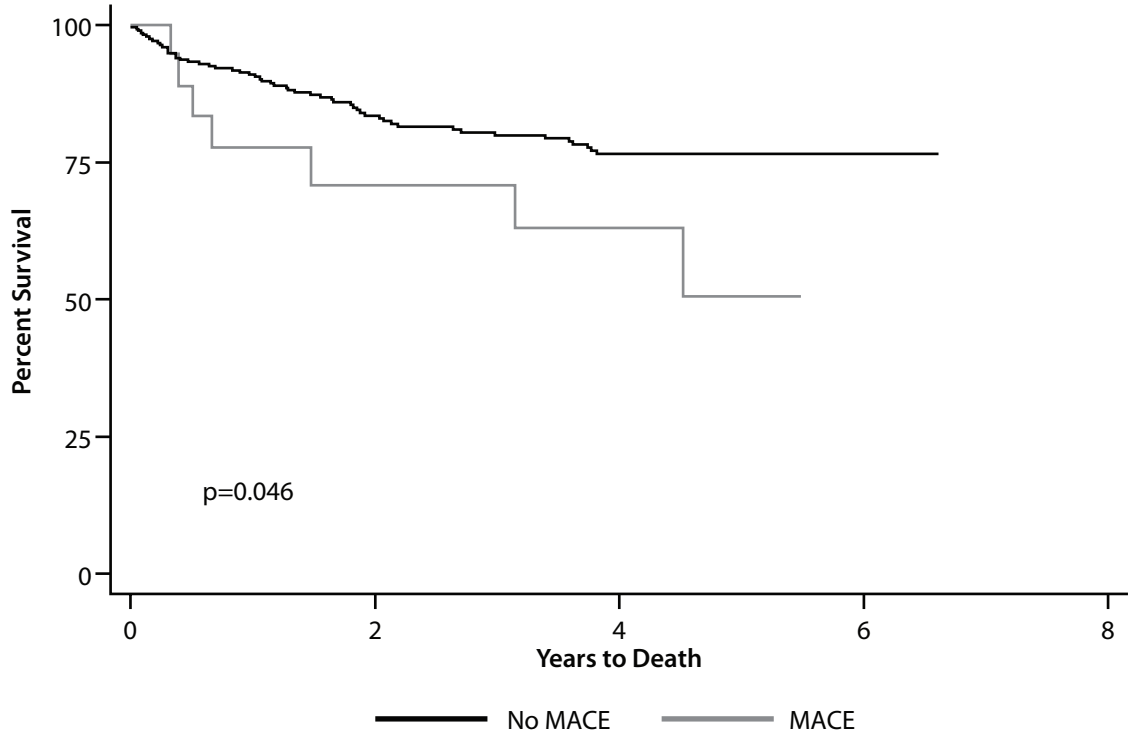
Background: Acalabrutinib is a highly selective second-generation Bruton's tyrosine kinase (BTK) inhibitor approved for the treatment of chronic lymphocytic leukemia (CLL) and mantle cell lymphoma. Ibrutinib, the first-generation nonselective BTK inhibitor, has been associated with cardiovascular (CV) complications including atrial fibrillation and ventricular arrhythmias, potentially related to off-target effects. In prior studies, the incidence of major adverse cardiovascular effects (MACE) with ibrutinib was 16.5–38%. With acalabrutinib being more selective, we postulate that less of these off-target effects would be seen. Although early experience with acalabrutinib suggests improved tolerability compared to ibrutinib, the long-term CV risks are unknown. Therefore, we sought to characterize the incidence, risk factors, and management of CV complications associated with acalabrutinib across long-term follow-up.

Methods: We performed a retrospective single-center cohort study of adult patients treated with acalabrutinib for a hematologic malignancy from January 2010 to August 2019. Patient demographics, CV and cancer variables, and CV complications were collected throughout the duration of acalabrutinib therapy. MACE was defined as cardiac arrhythmias (including atrial and ventricular arrhythmias), myocardial infarction, stroke, heart failure, and CV death. CV events, including arrhythmias, were graded according to the Common Terminology Criteria for Adverse Events (CTCAE), and adjudicated with an independent cardiologist. Descriptive statistics were used to summarize patient characteristics, using the mean ± standard deviation (SD) or median (interquartile range) for continuous variables and frequency counts with percentages for categorical variables. Time-to-event analysis methods were used to summarize MACE outcomes and evaluate associations with these outcomes.

Results: Overall, 290 patients treated with acalabrutinib were identified, majority had CLL (89%), and were male (72%) with a median age of 64 years. Seventy-seven (27%) patients were previously treated with ibrutinib. Sixty-seven percent of patients had a prior cardiac history, including 49% with baseline hypertension (HTN). MACE occurred in 18 patients (6%). Atrial fibrillation was the most common event occurring in 12 patients, followed by diastolic heart failure in 3 patients. There was one ventricular arrhythmic event (0.3%). Forty-four percent of patients temporarily held acalabrutinib during the MACE event, while 50% had no change to their acalabrutinib therapy. After the event, 6% of patients discontinued acalabrutinib and 11% of patients had dose reduced to 100mg daily. Age, gender, diabetes, kidney disease, and smoking status were found to be significantly associated with MACE. The odds of MACE were 1.8 times higher for every 7-year increase in age; when looking at just atrial fibrillation, the odds were 1.58 times higher for every 7-year increase in age. The effect of current smokers compared to never smokers was not significantly associated with MACE, however the odds of MACE were 3.4 higher in former smokers compared to never smokers. In comparison to ibrutinib (Dickerson, et al. Blood, 2019), the rate of MACE was lower- 66 vs 21 events per 1,000 person-years ($P<0.05$). Of the patients who developed MACE during acalabrutinib treatment, 7 (39%) died. Causes of death were related to infection, respiratory failure, or progression to hospice care. For survival outcomes, 79% of patients were expected to be alive at 3 years post acalabrutinib therapy, and 75% at 5 years. Among patients who experienced a MACE event, survival outcomes were worse ($P=0.046$), with 71% of patients expected to be alive at 3 years compared to 50% at 5 years (**Figure**).

Conclusion: In summary, acalabrutinib was associated with a lower, but significant risk of MACE compared to ibrutinib. The occurrence of these cardiac events appears to associate with worse survival outcomes. Further research into the mechanism(s) of these events, their implications, and the optimal preventative strategies for adverse CV complications after BTK inhibitor initiation is needed.

Figure. Overall Survival by MACE



Disclosures: Blachly: *AbbVie, AstraZeneca, KITE Pharma:* Consultancy. **Rogers:** *Genentech:* Research Funding; *Acerta Pharma:* Consultancy; *Pharmacyclics:* Consultancy; *AstraZeneca:* Consultancy, Other: Travel Funding; *Janssen:* Research Funding; *AbbVie:* Consultancy, Research Funding. **Byrd:** *Kartos Therapeutics:* Research Funding; *Trillium:* Research Funding; *Vincera:* Research Funding; *Novartis:* Research Funding; *Acerta Pharma:* Research Funding; *Syndax:* Research Funding; *Leukemia and Lymphoma Society:* Other; *Janssen:* Consultancy; *Pharmacyclics LLC, an AbbVie Company, Gilead, TG Therapeutics, BeiGene:* Research Funding; *Pharmacyclics LLC, an AbbVie Company, Gilead, TG Therapeutics, Novartis, Janssen:* Speakers Bureau; *Pharmacyclics LLC, an AbbVie Company, Janssen, Novartis, Gilead, TG Therapeutics:* Other. **Woyach:** *AbbVie:* Research Funding; *Janssen:* Consultancy, Research Funding; *Karyopharm:* Research Funding; *Loxo:* Research Funding; *Morphosys:* Research Funding; *Pharmacyclics:* Consultancy, Research Funding; *Verastem:* Research Funding.

Abstract 1317

Adverse Events in Clinical Trials of Ibrutinib and Acalabrutinib for B-Cell Lymphoproliferative Disorders: A Systematic Review and Network Meta-Analysis

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Introduction: Bruton tyrosine kinase (BTK) inhibitors are a class of drugs that inhibit B-cell receptor (BCR) and are increasingly used in B-cell lymphoproliferative neoplasms, including chronic lymphocytic leukemia (CLL), mantle cell lymphoma (MCL), and Waldenstrom's macroglobulinemia. Ibrutinib, a first-generation BTK inhibitor has been associated with increased risk of cardiovascular adverse events (AEs), including atrial fibrillation (AF), hypertension (HTN) and bleeding. These unique AEs are thought to be due to off-target effects. Acalabrutinib, a second-generation BTK inhibitor is characterized by less off-target effects, and is thought to be associated with a decreased risk of cardiovascular and other AEs. However, a head to head comparison of ibrutinib and acalabrutinib has not been conducted. Herein, we conducted a systematic review and network meta-analysis of AEs from prospective clinical trials of ibrutinib and acalabrutinib in B-cell lymphoproliferative disorders to compare their safety profile.

Methods: We searched PubMed, Embase, Scopus, and Web of Science from database inception through November 15th 2019. Only full-text articles were included. Other inclusion criteria included prospective trials (single arm or randomized) with ibrutinib, ibrutinib plus anti-CD20 antibody, or acalabrutinib as investigational agents. Trials investigating BTK inhibitor plus chemotherapy were excluded. When updated results of prospective trials were available, data were extracted from the most recent publication with the longest follow-up. Reports of 17 AEs of interest, including number of events (any grade and grade 3 or higher) were documented. Rate of discontinuation was investigated.

Results: Twenty-seven prospective clinical trials, 12 multicenter single-arm, 9 multicenter randomized, 5 single center single-arm, and 1 single center randomized, were included. Data from 29 study arms including 3207 patients were analyzed in 3 groups – ibrutinib, ibrutinib plus anti-CD20 antibody, and acalabrutinib with augmented Bayesian network meta-analysis and meta-regression implemented in R including packages *gemtc* and *rjags*. The most common any grade AEs (>20%) with ibrutinib were diarrhea (46%, 95% CI 36–55%), myalgias/arthralgias (37%, 95%CI 28–46%), fatigue (33%, 95% CI 24–42%), cough (26%, 95% 17–36%), anemia (23%, 95% 15–30%), thrombocytopenia (22%, 95% 15–30%), and pyrexia (21%, 95% 13–30%). The most common any grade AEs with acalabrutinib were headache (37%, 95% CI 26–48%), diarrhea (30%, 95% 20–41%), peripheral edema (21%, 95% 15–28%), fatigue (20%, 95% 11–29%), and myalgias/arthralgias (16%, 95% 8–24%). The most common any grade cardiovascular AEs with ibrutinib were bleeding/bruising (32%, 95% 23–41%), HTN (23%, 95% 15–32%), AF (9%, 95% 3–15%). The most common any grade cardiovascular AEs with acalabrutinib were bleeding/bruising (41%, 95% CI 30–52%), and HTN (6%, 95% 1–11%).

The rate of AEs with ibrutinib compared to ibrutinib plus anti-CD20 antibody were similar so the data was pooled. Of all AEs of interest, there was a significant difference in any grade AEs favoring ibrutinib for headache (12% vs. 37%), and infections (35% vs 57%). There was a significant difference in any grade AEs favoring acalabrutinib for myalgias/arthralgias (16% vs. 37%), anemia (6% vs. 23%), thrombocytopenia (5% vs. 22%), and HTN (6% vs. 23%). After adjusting for median follow-up and age, there was no significant difference in rates of bleeding/bruising and any grade infections between ibrutinib and acalabrutinib. However, there was a significant difference favoring acalabrutinib for any grade HTN (OR 0.26, 95% CI 0.17–0.40) *p<0.0001*, grade 3 HTN (OR 0.15, 95% 0.08–0.27) *p<0.0001*, any grade AF (OR 0.35, 95% 0.18–0.66), *p=0.0012*, grade 3 AF (OR 0.04, 95% 0.01–0.25) *p=0.0009*, and grade 3 infections (OR 0.62, 95% 0.46–0.85), *p=0.003*.

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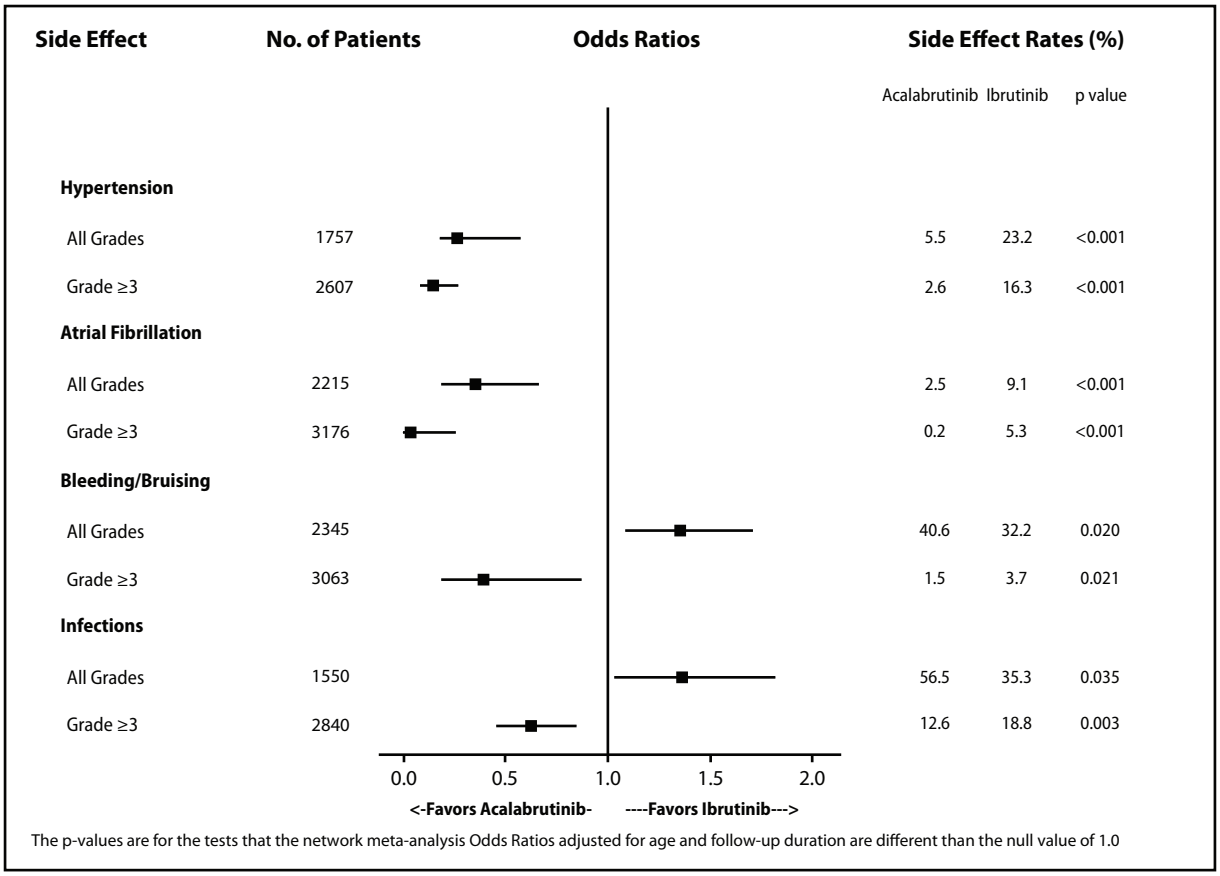
Conclusions: Acalabrutinib appears to have an overall improved safety profile compared to ibrutinib. This is particularly true for anemia, thrombocytopenia, and cardiovascular AEs, including AF and HTN.



Disclosures: No relevant conflicts of interest to declare.

FACHKURZINFORMATION

▼Dieses Arzneimittel unterliegt einer zusätzlichen Überwachung. Dies ermöglicht eine schnelle Identifizierung neuer Erkenntnisse über die Sicherheit. Angehörige von Gesundheitsberufen sind aufgefordert, jeden Verdachtsfall einer Nebenwirkung zu melden. Hinweise zur Meldung von Nebenwirkungen, siehe Abschnitt 4.8 der Fachinfomation.

BEZEICHNUNG DES ARZNEIMITTELS: Calquence 100 mg Hartkapseln. **Pharmakotherapeutische Gruppe:** Antineoplastische Mittel, Proteinkinase-Inhibitoren. **ATC Code:** L01XE51. **QUALITATIVE UND QUANTITATIVE ZUSAMMENSETZUNG:** Jede Hartkapsel enthält 100 mg Acalabrutinib. **Sonstige Bestandteile:** Kapselinhalt: Mikrokristalline Cellulose, Hochdisperses Siliciumdioxid, Vorverkleisterte Stärke (Mais), Magnesiumstearat (E470b), Poly(O-carboxymethyl)stärke-Natriumsalz. Kapselhülle: Gelatine, Titandioxid (E171), Eisen(III)-oxid-hydroxid x H2O (E172), Indigocarmin (E132). Drucktinte: Schellack, Eisen(II,III)-oxid (E172), Propylenglycol (E1520), Ammoniak-Lösung. **ANWENDUNGSGEBIETE:** Calquence als Monotherapie oder in Kombination mit Obinutuzumab ist zur Behandlung von erwachsenen Patienten mit nicht vorbehandelter chronischer lymphatischer Leukämie (CLL) indiziert. Calquence als Monotherapie ist zur Behandlung von erwachsenen Patienten mit chronischer lymphatischer Leukämie (CLL) indiziert, die mindestens eine Vorbehandlung erhalten haben. **GEGENANZEIGEN:** Überempfindlichkeit gegen den Wirkstoff oder einen der in Abschnitt 6.1 der Fachinformation genannten sonstigen Bestandteile. **INHABER DER ZULASSUNG:** AstraZeneca AB, SE-151 85 Södertälje, Schweden. **REZEPTPFLICHT/ APOTHEKENPFLICHT:** Rezept- und apothekenpflichtig, wiederholte Abgabe verboten. **STAND DER INFORMATION:** 11/2020.

Informationen zu den Abschnitten besondere Warnhinweise und Vorsichtsmaßnahmen für die Anwendung, Wechselwirkungen mit anderen Arzneimitteln und sonstige Wechselwirkungen, Fertilität, Schwangerschaft und Stillzeit, Nebenwirkungen sowie den Gewöhnungseffekten sind der veröffentlichten Fachinformation (z. B. Austria Codex) zu entnehmen.

Springer Healthcare

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Printed in Germany

ASZ20DV005003

AT-4272 11/2020