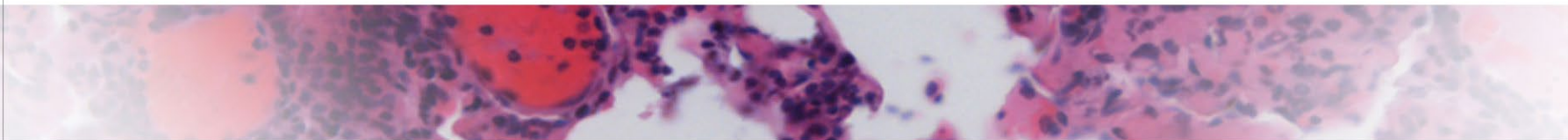




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Management of BTK Inhibitor Associated Adverse Events: Current Practice Trends Among Healthcare Providers and Concordance With Expert Recommendations

Kristen Rosenthal, PhD^{1*}; Jeremy S Abramson, MD, MMSc²; Farrukh T Awan, MD³; John P. Leonard, MD^{4,5}; Julie M. Vose, MD, MBA⁶; Timothy A Quill, PhD^{1*}; and Christopher Flowers, MD⁷

¹Clinical Care Options, LLC, Reston, VA; ²Massachusetts General Hospital Cancer Center, Boston, MA; ³University of Texas Southwestern Medical Center, Dallas, TX;
⁴Weill Cornell Medical College, New York, NY; ⁵Weill Cornell Medical College, Pelham Manor, NY; ⁶University of Nebraska Medical Center Fred & Pamela Buffett Cancer Center, Omaha, NE;
⁷The University of Texas MD Anderson Cancer Center, Houston, Texas

Disclosures

- **Kristen M. Rosenthal, PhD**, has no relevant financial relationships to disclose.
- **Jeremy S. Abramson, MD, MMSc**, has no relevant financial relationships to disclose.
- **Farrukh T. Awan, MD**, has served as consultant for AbbVie, AstraZeneca, Blueprint Medicines, Celgene, Dava Oncology, Genentech, Gilead Sciences, Janssen, Karyopharm, Kite, MEI Pharma, Pharmacyclics, and Sunesis.
- **John P. Leonard, MD**, has served as consultant for ADC Therapeutics, AstraZeneca, Bayer, Bristol-Myers Squibb/Celgene, Epizyme, Genmab, Gilead Sciences/Kite, Karyopharm, MEI Pharma, Miltenyi, Sutro, Regeneron, and Roche/Genentech.
- **Julie M. Vose, MD, MBA**, has served as consultant for AbbVie, AstraZeneca, Karyopharm, Loxo, Roche/Genentech, and Verastem; has received honoraria from AbbVie, Allogene, AstraZeneca, Celgene, Epizyme, Janssen, Karyopharm, Miltenyi Biotech, Loxo, Roche/Genentech, Wugen, and Verastem; and has received funds or research support from AstraZeneca, Bristol-Myers Squibb, Epizyme, Incyte, Kite/Gilead, Loxo, Novartis, and Seattle Genetics.
- **Timothy A. Quill, PhD**, has no relevant financial relationships to disclose.
- **Christopher Flowers, MD**, has served as consultant for AbbVie, Bayer, BeiGene, Celgene, Denovo, Genentech/Hoffmann-La Roche, Gilead Sciences, Karyopharm, Pharmacyclics/Janssen, OptumRx, and Spectrum and has received funds for research support from AbbVie, Acerta, Burroughs Wellcome Fund, Celgene, Eastern Cooperative Oncology Group, Genentech/Hoffmann-La Roche, Gilead Sciences, Millennium/Takeda, National Cancer Institute, TG Therapeutics, and V Foundation.



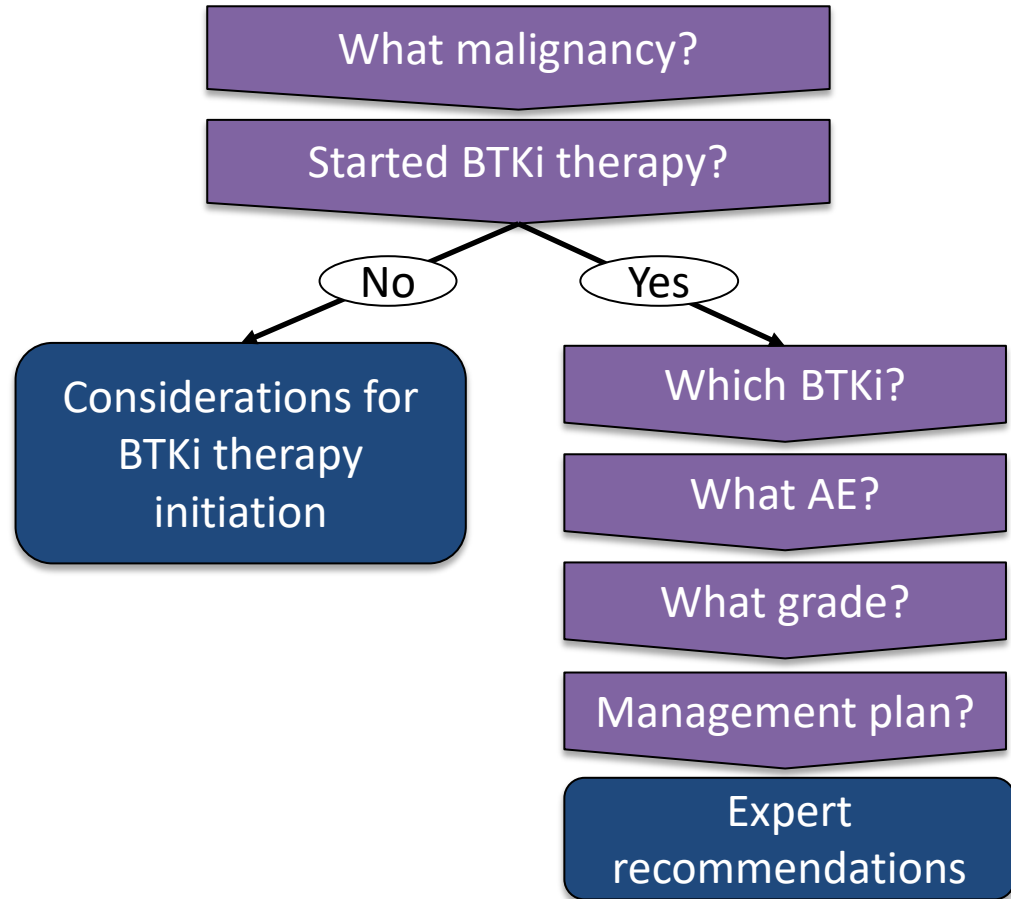
Background

- The advent of BTK inhibitors (BTKi; ibrutinib, acalabrutinib, zanubrutinib) has dramatically improved outcomes for many patients with B-cell malignancies
- To ensure optimal patient outcomes with BTKi therapy, it is essential to maintain both ongoing therapy and patient quality of life
 - These dual goals require prompt recognition and management of the unique adverse events (AEs) associated with BTKi therapy
- In 2019, we developed an online decision support tool to provide case specific guidance on managing BTKi AEs
- Here, we report data from this tool comparing expert recommendations and community HCPs management plans for defined patient scenarios



Tool Development

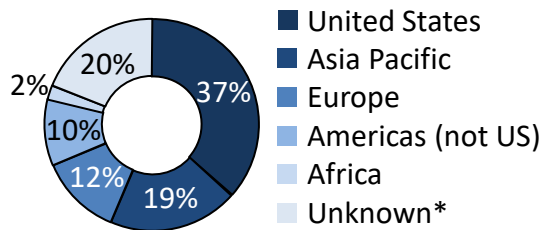
- 5 experts identified a simplified set of key questions on BTKi AEs
 - **Experts:** Jeremy S. Abramson, MD, MMSc; Farrukh T. Awan, MD; John P. Leonard, MD; Julie M. Vose, MD, MBA; and Christopher Flowers, MD
- In July 2019, these experts provided recommendations for managing distinct AE scenarios arising from the different combinations of the chosen characteristics



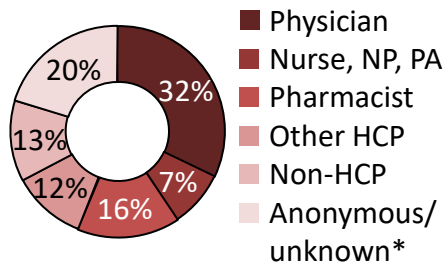
Demographics of Tool Participants: September 2019 - October 2020

- 970 complete cases entered by 532 distinct individuals

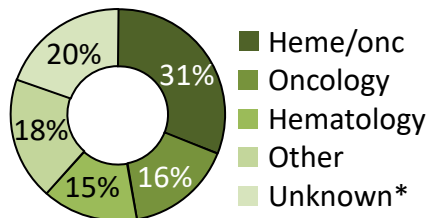
Geographic Distribution



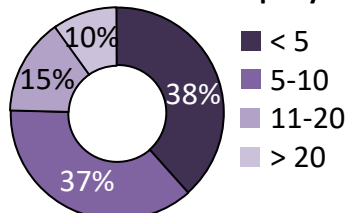
Role/Degree



Specialty



How many patients do you treat with a BTK inhibitor per year?



Optional survey (N = 100)

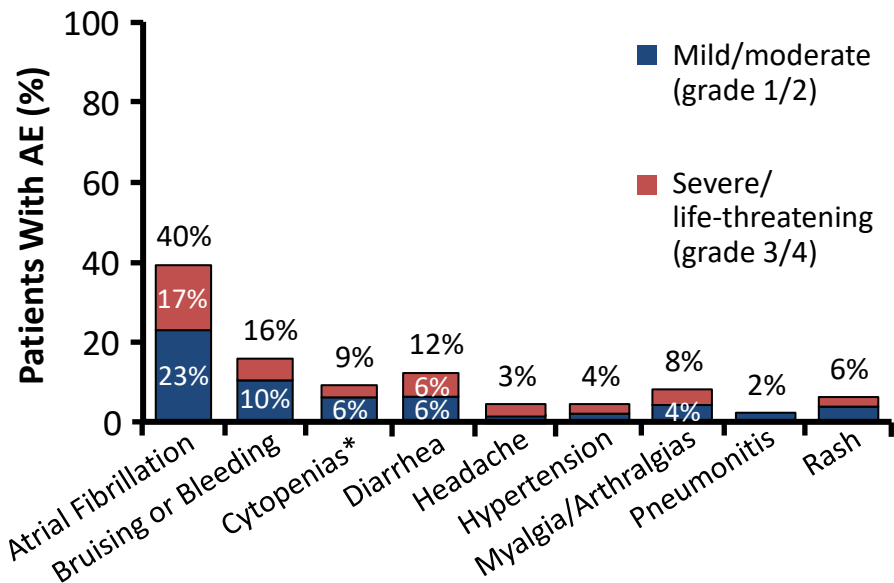
Disease Entered	Cases From All Participants, n (%)	Cases From HCP Participants, n (%)
CLL	679 (70)	485 (73)
MCL	159 (16)	100 (16)
MZL	58 (6)	33 (6)
WM	71 (7)	45 (7)

Begun BTKi Tx?	Cases From All Participants, n (%)	Cases From HCP Participants, n (%)
No, Tx is planned	450 (47)	306 (46)
Yes	517 (53)	357 (54)
• Experiencing AE	429	301
• Planning medical procedure	88	56

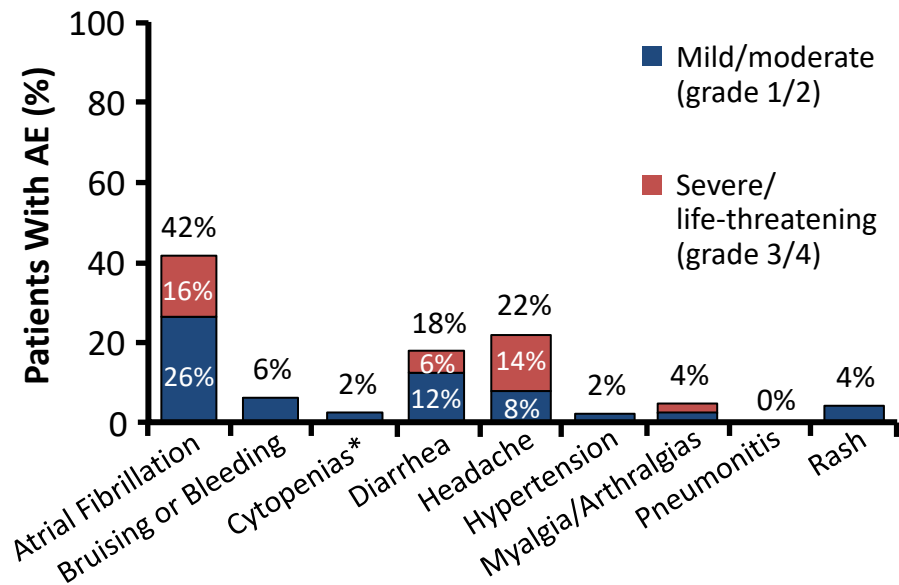


Patient Cases Entered Into Tool by HCPs: Type of AE (N = 301)

Ibrutinib (n = 251)



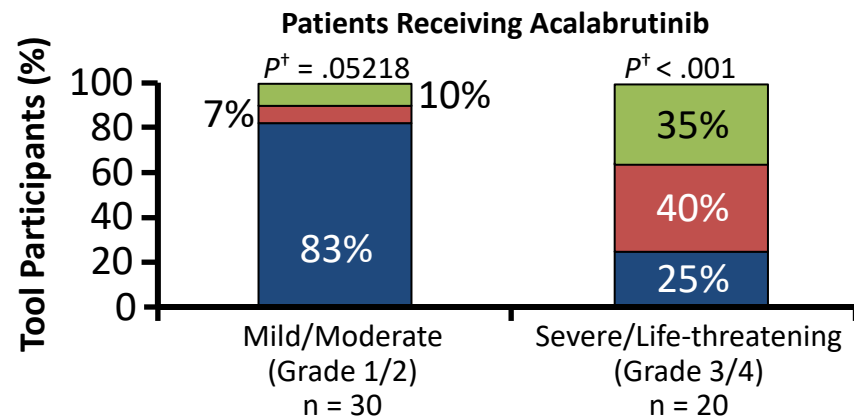
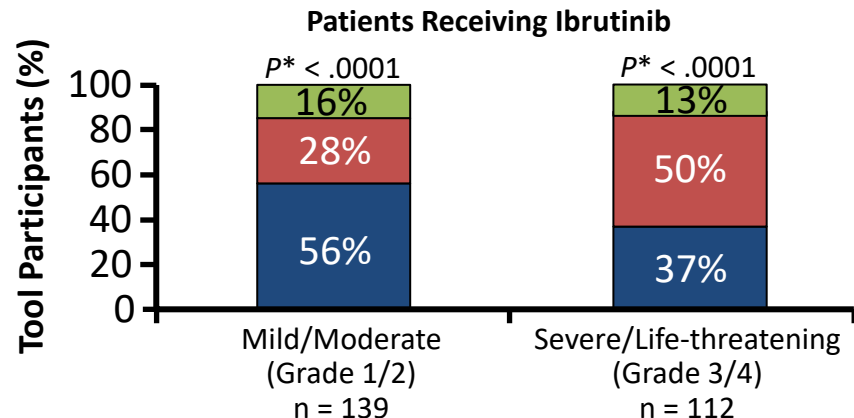
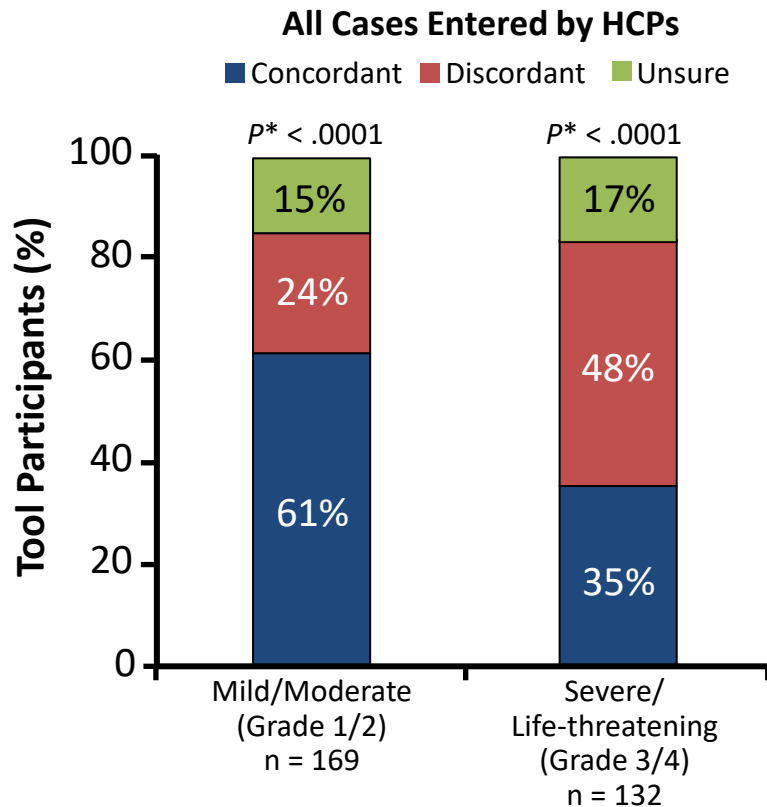
Acalabrutinib (n = 50)



*Mild/moderate includes grade 1-3 cytopenias and severe/life-threatening includes grade 3 neutropenia with infection or fever or grade 4 cytopenias. †Severe/life-threatening includes grade 3 thrombocytopenia with bleeding, grade 4 thrombocytopenia, and grade 4 neutropenia lasting longer than 7 days and mild/moderate includes any other cytopenias.

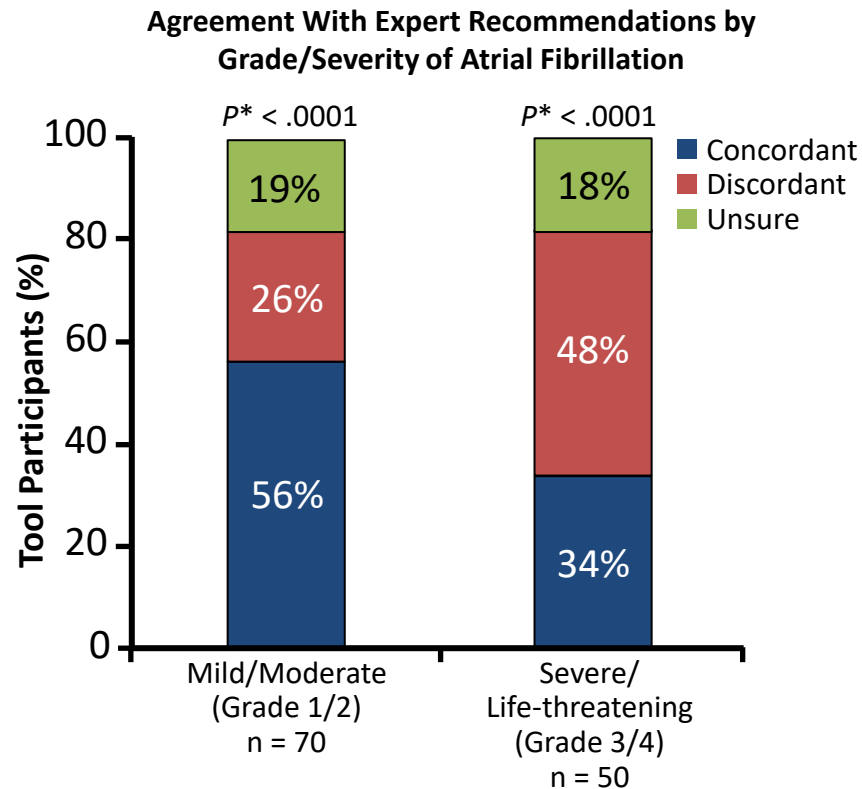


HCP Agreement With Expert Recommendations



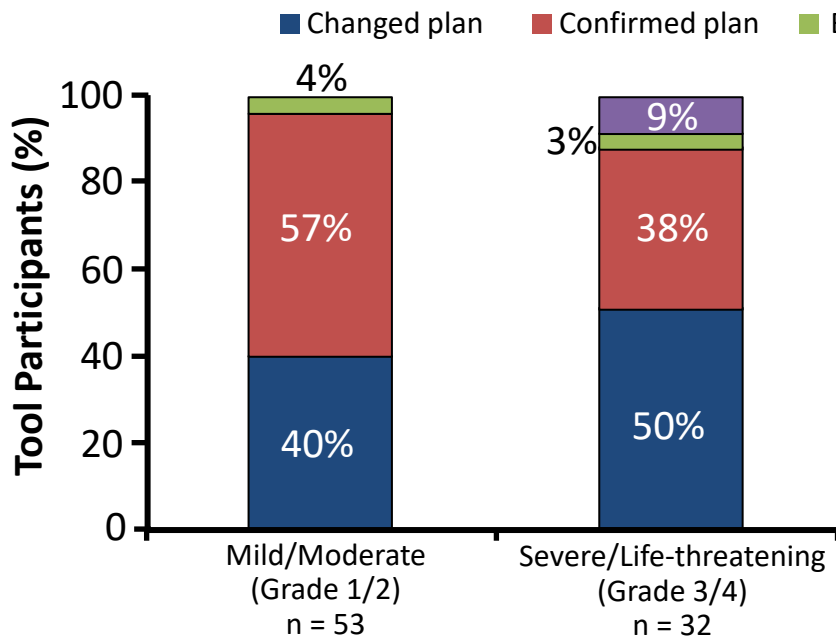
Example: Management of Atrial Fibrillation

Expert Recommendations	Summary
Grade 1/2	<ul style="list-style-type: none"> • Cardiology consult • Treatment with BTKi can generally be continued while rate control-directed therapeutic interventions are initiated • Use of concurrent anticoagulant therapy needs to be assessed on a case-by-case basis
Grade 3/4	<ul style="list-style-type: none"> • Cardiology consult • Hold BTKi until symptoms resolve and there is adequate rate control • After clinical resolution to grade < 3 or baseline, BTKi can be resumed at the same dose for the first occurrence or can be dose reduced for recurrences • Discontinue for recurrence after dose reductions (per package insert)

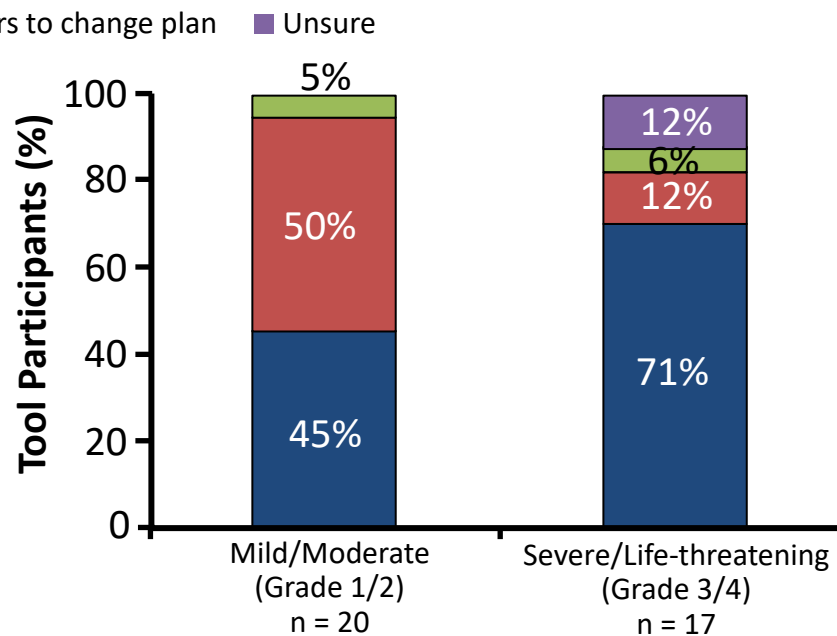


Impact of Tool on Planned HCP Clinical Practice

Optional Survey: Did the Expert Recommendations Change Your Management Approach?



HCPs Whose Management Plan Was Different Than Expert Recommendations



Conclusions

- In our online tool on managing BTKi AEs, 75% of clinicians indicated that they treat ≤ 10 patients/yr with a BTKi
- Most common AEs ($\geq 10\%$) entered regardless of BTKi choice were atrial fibrillation, diarrhea, and bruising or bleeding
 - Headache was also a commonly entered for acalabrutinib
- Management of BTKi AEs by HCPs often diverges from evidence-based expert recommendations, especially grade 3/4 AEs
 - For grade 1/2 AEs, 24% did not match expert recommendations and 15% were unsure
 - For grade 3/4 AEs, 48% did not match expert recommendations and 17% were unsure
- Use of an online tool providing easy access to BTKi AE management recommendations may improve patient care and safety
 - For HCPs whose plans differed from expert recommendations, 71% would change their management approach for grade 3/4 AEs based on the information from this tool

