[AN HCG OPINION PIECE]

ASH 2024 NAVIGATOR

Unlocking key takeaways in non-malignant hematology

As one of the key end-of-the-season conferences, ASH has always held a special place in our heart as a last chance to connect across hematology on everything from oncology to rare disease. At ASH 2024 in San Diego, we navigated a sprawling program to find the hidden gems in non-malignant hematology and the major themes driving clinical decision-making.

Precision medicine–from trend to clinical practice

ASH is known as a conference with no shortage of data on the latest innovations in hematology, and the 2024 event certainly lived up to that reputation, with presentations from basic science, proof-of-concept, and pivotal trial data across the spectrum of innovative therapeutics. A particular focus on the non-malignant program was on the strides that have taken place in tackling rare conditions such as hemophilia, immune thrombocytopenia (ITP), and sickle cell disease (SCD). With a plethora of new options on the horizon, discussions turned to how to deliver this innovation and the promise of "precision medicine" to patients.

Considerations ranged from identification of suitable patients, through monitoring outcomes (and defining "success"), to the practicalities of incorporating new options into existing hospital systems.

In ITP, for example, physicians can see the potential to adopt approaches that rely on a rational combination of therapies based on different mechanisms of action, but clinical trials and real-world data are often lacking, and these combinations are not included in current treatment guidelines, resulting in limited ability to offer them in usual-care settings.

Another area where the promise of precision medicine meets the practical reality of clinical care is when it comes to data for specific patient populations, such as older adults and pregnant women (where the unborn child is also a "patient"). With this mind, it's our opinion that precision medicine approaches could benefit from clinical

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trial programs that go further for all patients by considering what additional data they can provide beyond the trial itself (especially in trials of rare diseases with small patient numbers). Efforts such as exploration of indirect comparisons, greater investment in modelling data, meta and post hoc analyses, sharing and making available data from post-marketing surveillance, and industry support for clinic-based and national real-world evidence collection approaches all have potential merit.

> Precision medicine approaches could benefit from clinical trial programs that go further for all patients by considering what additional data they can provide beyond the trial itself

Returning to the discussion at ASH, another example shared during the congress that may help get us closer to the promise of precision medicine is the progress being made in gene therapy for patients with SCD. Data and approaches shared help illustrate the value of novel study design to inform more precision approaches to evaluating innovative therapeutics. For the *ex vivo* gene therapy (lovo-cel), post hoc analysis of patients enrolled into two clinical studies helped generate data on predictors of outcome to inform both new patient selection and the manufacturing/testing of the personalized cell therapy product. In effect, this optimizes trial design to help identify key product parameters predictive of a positive outcome.

Shared decision-making in a changing landscape

Another trend that emerged clearly for us—across both the malignant and non-malignant programs—was the value of physician education and awareness of novel, innovative treatments that go beyond simply "CME." In an increasingly innovative treatment landscape, the need for physicians and care teams to do more to support shared decision-making with patients has come to the fore. Particularly, this is seen in efforts to engage patients directly to understand the evolving landscape, often in situations where physicians themselves may not yet have had time to build a solid educational foundation.

We are strong believers in the need for more support and education for care teams to help drive open dialog around treatment "choice," with consideration of patient (including caregiver/family) values and perspectives. In particular, the need to integrate this approach "as-standard" into companies' stakeholder engagement plans requires more focus.

At ASH 2024, we honed in on emerging trends and efforts, such as investment in plain language summaries to support transparent communications and how to communicate negative trial results. We also noted a new track at ASH that featured poster and oral presentations dedicated to improving HCP and patient education and communications across the hematology landscape.

> Patients are being engaged to help in understanding the evolving treatment landscape—often in situations where their physician hasn't yet had the time to build a strong educational foundation

And it's not just the patient who requires additional support to connect with evolving study outcomes and more complex data sets. An increased focus on patient-reported outcomes (PRO) was highlighted as particularly challenging to interpret and present. Across a number of sessions, we saw unclear messaging and statistical techniques that were complex to understand (and explain). However, in the poster hall, indicators of how to better communicate these data came to life—particularly the value of impactful qualitative quotes to complement more quantitative PRO data when sharing study results. Whilst this marks a clear move to more accessible data communication (especially in the historically data-heavy poster format), more can and should be done to bring these complex data sets and endpoints to life—for all audiences.

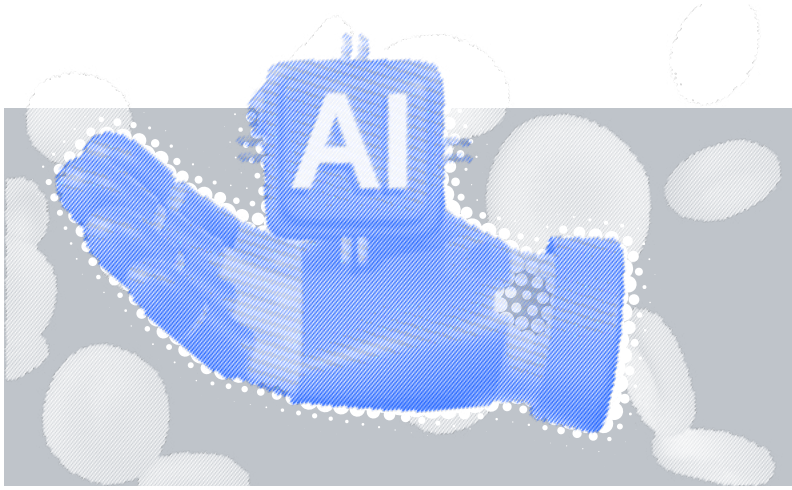
Especially because, as approval of innovative therapeutics increases and the field becomes more and more crowded, the question of "choice" will likely move from "*should* I take a more experimental, innovative treatment (such as gene therapy)" to "*which* should I choose?"

In the absence of head-to-head data, physicians will naturally use existing publications to compare products, regardless of differences in study designs and populations—as was seen in some hemophilia sessions this year at ASH. It's clear we need to find better mechanisms to address this natural need to "compare" if we are to support patient engagement and "choice."

Hematology and AI—where are we now?

A congress in the present day wouldn't be a congress without sessions focused on AI, and ASH 2024 was no different. Both practical and ethical aspects of AI—including sustainability considerations—were addressed in various sessions.

In non-malignant hematology, a variety of posters presented AI, including large-language and analytical models being used for diagnosis and prognosis and to help to manage hematologist workloads by supporting with triage, treatment decisions, and communication. A particular highlight was an innovative approach shared in



the rare disease, wAIHA, which used AI to run "sentiment analysis" from online communications to help identify patient concerns and topics of interest to inform future education and support.

Our ASH 2024 hidden gem

Speaking of what we can learn from rare disease, we want to close out our opinion piece for another year by highlighting what we believe is one of the great joys of ASH—the hidden gems one finds in an otherwise predictable session. In 2024, for us, this was a short presentation by Dr Hanny Al-Samkari during the ASH–FDA joint symposium. He illustrated the wider community impact of clinical development in ultra-rare disease: as a result of the development of mavorixafor, the WHIM syndrome community not only has a new therapy but also a company-provided genetic diagnosis service, a disease registry, *and* a patient support group. And the broader healthcare community now has a new drug being tested in other neutropenia disorders. We love it when a plan comes together! ■

Abbreviations

wAIHA, warm autoimmune hemolytic anemia;
WHIM, warts, hypogammaglobulinemia, infections, and myelokathexis.

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