Endpoints in Drug Development

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Continued need for novel oncology endpoints

Increased patient centricity

- Need for endpoints that can more fully address quality of life, symptom control and functional improvement, ensuring patient centric evaluation
- Current endpoints (or approaches) may not reflect benefits in rare or heterogeneous cancers

Harness advances in science

- Scientific advances drive more personalized medicine/ targeted approaches
- Shift towards earlier treatment settings, with novel curative intent
- Advances in imaging, tumor-detection and artificial intelligence, allowing measurement of novel endpoint concepts

Enabling patient access

- Need for faster assessments compared to overall survival
- Due to improved survival times, intermediate endpoints are needed to support timely access and approval
- Need for endpoints to evaluate safety
- Novel endpoints help demonstrate the real-world value of therapies

While progress has been made, challenges and opportunities remain

Development of novel endpoints is time intensive

- Discussions around MRD as an endpoint began before 2012, US guidance released in 2020, MRD ODAC as an endpoint in multiple myeloma clinical trials in 2024, EMA interactions ongoing
- Accelerated/Conditional Approval pathways provide opportunities to enable earlier access using clinically meaningful intermediate and surrogate endpoints.

Need for Fit for Purpose pathways

- Review pathways and opportunities to engage with Health Agencies for endpoints developed outside an IND
- EMA Qualification of Novel Methodologies procedure being reviewed
- CTR/IVDR interface impacting the ability to conduct precision medicine clinical trials in the EU due to a lack of harmonisation and capacity for assessment

Guidance needed on novel approaches and specific cancer types

- Advances in imaging and AI support the development of novel endpoints but guidance has not been developed by all health authorities
- Guidance on specific cancer types, patient subsets, and therapeutic niches only exists in some disease areas

Incorporation of patient experience data

- Lack of clarity regarding regulatory perspectives on patient experience data (e.g., PROs) and incorporation into regulatory decision-making and labelling (particularly for open-label studies)
- Proposal for new ICH guideline on Patient Experience Data provides globally harmonised approach to inclusion of PED to inform regulatory decision making

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Mission

Accelerate the development and delivery of novel life-extending therapies to patients with AML by establishing MRD as a new clinical endpoint

MPAACT: MRD partnership and alliance in AML clinical treatments

Learnings

- Required to have a significant number of RCT for meta-analysis
  - For patient and trial level analysis
  - Defining MRD endpoint candidate
  - Timepoints and window of assessment
  - Threshold of classifying MRD negativity
- Require an external statistical group to conduct meta-analysis
- Methodology: Technology used to assess MRD

Opportunities for progress

- Academic investigators and industry collaboration critical.
- Early Engagement with regulatory authorities and HTAs is critical for the project's success
- Inclusion of patient advocacy groups important
- Systemic Literature Review provides insight into new published RCT studies with endpoint inclusion
- More guidance on establishing early clinical endpoints in all disease settings required from regulators
- Joint workshops with regulators, pharma, academics on this topic very much needed

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