ISSUE PANEL

Clinical Evidence for Health Technology Assessment in Oncology, Are We Going Backwards?

Where Are We Going With Single-arm Trials?

Tuesday, 8 November 2022 | 10:15-11:15
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Many products are receiving approval based on single-arm trials

• FDA granted 153 new oncology indications based on single-arm trials between 2001 and 2020.
  – 102 accelerated and 51 regular approvals
• 32 NICE oncology appraisals between 2017 and 2022 (17%) used only single-arm trial evidence as the primary clinical evidence.
  – 91% of these (29 of 32) were recommended for use
  – Half were within the Cancer Drugs Fund
Motivations commonly cited for the use of single-arm trials

- High unmet medical need
- Avoids allocating patients to potentially less effective control therapies
- Challenges with lengthy and confounded survival endpoints
- Difficulty enrolling patients with rare tumour types
  - e.g., biomarker-defined subsets of disease
Single-arm trial endpoints for regulatory approval

• **Response rate**
  – Most common endpoint used for substantial evidence of efficacy to support approval
  – 120 of 153 FDA approvals (78%)

• **Durability of response**
  – Also considered as supportive evidence of clinical benefit

• **Why not progression-free survival (PFS) or overall survival (OS)?**
  – Tumour regression (response) can be directly attributed to the drug(s)
    • Spontaneous remission is rare to non-existent (historical control: 0%)
  – “Prolonged” stable disease, PFS, and OS in a single-arm study could be due to natural history of the tumour and not the intervention

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Blumenthal. EMA-ESMO Workshop on single-arm trials for cancer drug market access. 2016.
Single-arm trial data presents challenges for health technology assessment (HTA)

- HTA requires comparison of new interventions with current treatments.
  - Indirect comparisons are required with outcomes from other trials or real-world data
  - Differences in costs and quality-adjusted life-years must be estimated over patients’ lifetimes
- Although statistical methods exist, there remains a substantial potential risk of bias.
  - Differences between studies in unknown or unmeasured prognostic factors
  - Differences between studies in the definition or ascertainment of endpoints
- Lifetime analyses require survival estimates.
  - Response endpoints may not be reliable surrogates for PFS or OS
- These issues, as well as small sample sizes, may result in substantial uncertainty in cost-effectiveness estimates.
Are we making progress towards higher quality clinical evidence for HTA in Oncology?

• Health economists and outcomes researchers have long called for evidence reflecting effectiveness in routine practice (e.g., pragmatic trials).
• Progress towards this approach has been very limited.
• Rather, with increased use of single-arm trials, are we going backwards?
Open debate –
Panel and audience (~15 min)

1 Panel presentations
- Vishal Bhatnagar, MD (FDA perspective)
- Adrian Vickers, PhD (Statistical perspective)
- Anne-Pierre Pickaert, MSc (A patient perspective)

2 Audience poll –
*With the increased use of single-arm trials as the primary evidence for oncology HTAs, are we going backwards?*
Many thanks to our panel and to you, the audience, for your thoughts!
It’s time for the poll!

With the increased use of single-arm trials as the primary evidence for oncology HTAs, are we going backwards?

- Yes
- No
- Maybe
- Don’t know
Join us to continue the discussion…

- Discussion group – 11:45 am today, Discussion Lounge, Exhibit Hall – X1

Look out for other sessions…

- Podium session 228 – 1:30 pm today, “Innovative Methods in Indirect Treatment Comparisons”
- Issue Panel 27 – 10 am tomorrow, “External Control Arms, Is It the Way to Go?”