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MANAGED ENTRY SCHEMES: HYPE VS. REALITY

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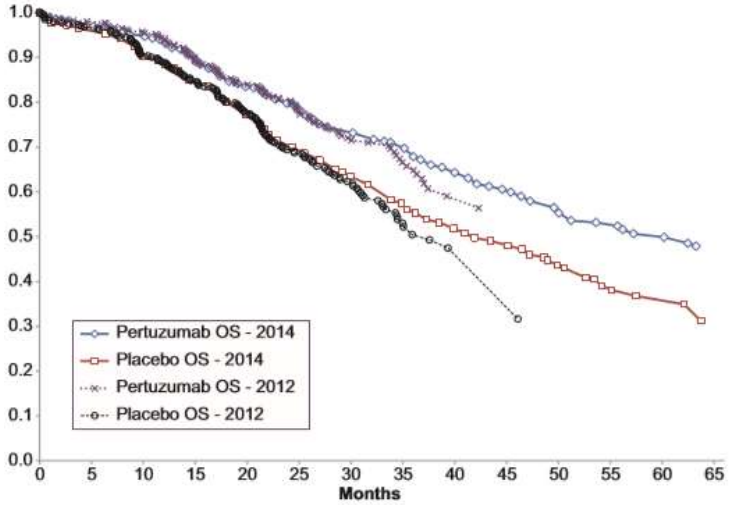
seek LIGHT

Background

- Relatively small patient populations, but not rare conditions
  - Long trial recruitment period
  - Predominantly cancer drugs
- Early evidence of positive treatment effect
  - Significant uncertainty around magnitude of gain in overall survival

Extrapolating OS is always uncertain & subjective



Bagust & Beale, 2018

- Key issue: convergence of OS curves:
  - Are curves less convergent at earlier datacuts?
  - Does earlier extrapolation predict larger OS gains?
- How should OS be analysed at interim datacuts?

England: the reformed Cancer Drug Fund

- Funding decision re-integrated with NICE
  - NICE appraises
  - If not recommended for routine funding, drugs can be passed onto the CDF
  - CDF provides interim funding, during period of additional data collection
    - Managed Access Agreements
  - NICE reappraises

CDF Activity update (to March 2018)

"Eighteen MAAs have been agreed within the new CDF.

Two MAA treatments have been reappraised by NICE, with additional clinical trial and real world data, as part of the CDF exit process.

Both treatments have been recommended for routine commissioning [*at what price, relative to price without managed access?*],

demonstrating the benefit of allowing earlier access … while further data is collected to evaluate their effectiveness"

Cancer Drug Fund – data collection

- Further follow-up of ongoing phase III, with comparator data
  - Ixazomib (multiple myeloma); Niraparib (ovarian cancer)
  - Osimertinib (NSCLC); Obinutuzumab (follicular lymphoma)
  - Olaratumab (sarcoma) + *SACT for treatment duration*
- Further follow-up of ongoing phase III, without comparator data
  - Atezolizumab (urothelial carcinoma); Avelumab (Merkel cell carcinoma)
  - Nivolumab (NSCLC)
- Analysis of Systemic Anti-Cancer Therapy (SACT) dataset
  - Crizotinib (NSCLC); Daratumumab (multiple myeloma)
  - Ibrutinib (Waldenström's macroglobulinaemia)
  - Venetoclax (lymphocytic leukaemia)

PBS MESs

- Crizotinib (NSCLC)
  - Sponsor collected 12m OS data
  - Target: 68.9% survival at 12m, validate submission survival analysis
- Trametinib (Melanoma)
  - Meta-analysis, with 2 additional years of follow-up for 1 trial
  - Reduction in clinical effect vs. submission – price reduction
- Pembrolizumab (Melanoma)
  - Extended follow-up of key clinical trial for 2 years
  - Data did not improve ICER - price equivalency with comparator maintained

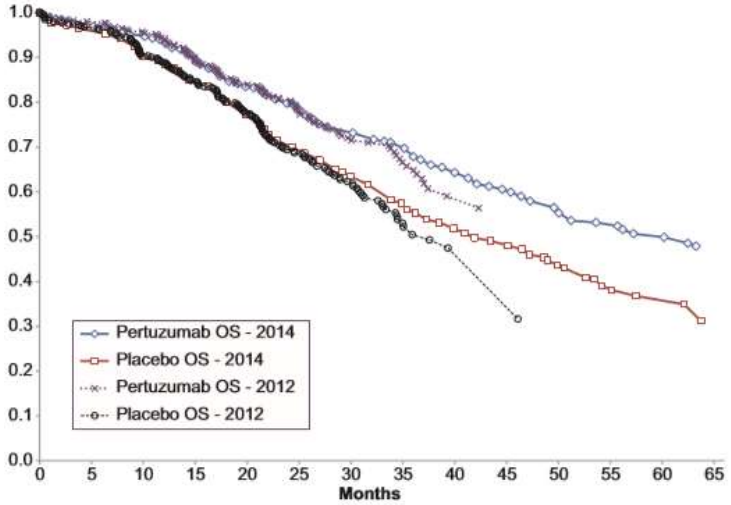
Tuffaha & Scuffham, 2018

Venetoclax (lymphocytic leukaemia)

- "PBAC noted the sponsor's advice that no more clinical data will be available for venetoclax monotherapy, thus the requirements for a Managed Access Program cannot be met."

- CDF:
  - SACT: time on treatment and overall survival, baseline characteristics of patients
  - Retrospective analysis of Best Supportive Care

Convergence of curves is key



- What does a crude comparison of real-world and trial OS at 12m or 2yrs, in the intervention arm, inform?
  - Differences between real-world and trial effects, in the intervention arm
  - False confidence in negative or positive result?

Bagust & Beale, 2018

PBAC: non-implemented proposed MESs

3: PBAC advised against proposed study: 2 listed, 1 not listed (Vaccine)

2: Sponsor argued against proposed MES: 2 listed

1: Sponsor reduced price: listed

Tuffaha & Scuffham, 2018

Non-informative MES vs. No MES

- Non-informative MES
  - Data collection costs
  - Price set too high if non-informative target achieved
  - Price set too low if non-informative target not achieved

- No MES
  - No data collection costs
  - Price set to reflect uncertainty

Recommendations

- Explore validity of comparisons using prospective intervention vs. retrospective comparator OS data
  - Value of routine Systemic Anti-Cancer Therapy dataset

- Investigate convergence of OS curves over time to inform interpretation of early extrapolation
  - To inform pricing that reflects uncertainty