Efficacy of second-line treatments in patients with metastatic hormone refractory prostate cancer (mHRPC) is not demonstrated by published evidence from non-randomised trials

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Background

- Novel drug-based chemotherapy is the currently standard 1st line treatment for patients with mHRPC.
- Few randomised clinical trials of 2nd line treatments after Docetaxel have been published to date with little evidence on survival and clinical benefit.
- At the time of the literature review there were no recommended second-line treatments for docetaxel pre-treated patients.

Objective

- The primary objective of this review was to assess the survival and clinical benefits of interventions in the treatment of second line metastatic hormone resistant prostate cancer (mHRPC).
- This review included all studies published in observational non-comparative or comparative prospective and retrospective studies.

Results

- Studies selection: 375 records were screened, and 32 studies were included in the review (Figure 1).

- For trials assessed the efficacy and safety of docetaxel re-challenge, after non-randomised or combination therapy, in the second-line treatment of mHRPC. Most of the included studies consisted of small, single-arm studies (seven studies). The 13 remaining studies evaluated other included interventions.

- The SLR showed a lack of available non-randomised evidence and among studies in the literature review demonstrates that it is difficult to infer the clinical efficacy of mHRPC 2nd line chemotherapy.

- Main findings:
  - Of the 32 included studies, only one was a comparative study. Small sample sizes were high in all but a few of the included studies enrolled fewer than 25 patients and 90% of included studies contained fewer than 50 patients.
  - Definitions of PFS and PSA response varied between the studies, and there were heterogeneity in terms of interventions, thus comparisons between the interventions were not possible.
  - For studies evaluating a challenge with Docetaxel, the median OS and PFS varied from 39-48 weeks and 13-16 weeks respectively.
  - For Mitoxantrone regimens based, the median OS and PFS varied from 38-49 weeks and 13-16 weeks respectively.
  - For other chemotherapy regimens, the median OS and PFS varied from 51-104 weeks and 9-17 weeks respectively.
  - PSA response rates varied from 24-70% to Docetaxel challenge, from 4-33% to Mitoxantrone based regimens and from 0-60% to other regimens.

Discussion

- This review did not publish a systematic literature review on observational trials in mHRPC was identified prior to this review.
- Limited non-randomized evidence was published in the ten-year period studied.
- Most data was non-comparative and included small sample size. Only one study out of 30 was comparative.
- In addition, different definitions for PFS and PSA response were used.
- Results appear to confirm clinical benefit of docetaxel re-challenge vs. mitoxantrone, but it needs to be studied cautiously.
- Based on the literature results, it is difficult to draw conclusions about the clinical efficacy of mHRPC 2nd line chemotherapy.

CONCLUSIONS

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