ICON7: ovarian cancer, platinum second-line chemotherapy and overall survival

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Background

The ICON7 trial reported increased progression-free survival with bevacizumab (bev) added to platinum-based chemotherapy in newly-diagnosed ovarian cancer, and increased overall survival (OS) in a poor prognosis subset. Most patients (pts) had further chemotherapy following progression. On average, pts receiving bev had later progression and were thus more likely to receive further platinum. We investigated the effect of second-line treatment type on the association between first-line bev and OS.

Methods

Second line chemotherapy regimens were categorised as platinum-containing or other. Platinum reuse varied with time to progression after end of 1st line (excl. maintenance bev) and also varied between centres. We categorised centres as high or low platinum use, from the proportion of their pts progressing in 0-8 months (mths) and retreated with platinum. The association between 1st line bev and OS was analysed separately at low-use centres and at high-use centres. Standard survival analysis techniques and methods appropriate for data with non-proportional hazards were used.

Results

ICON7 randomised 1528 pts 1:1 to reference treatment +/- bev. Reference pts were more likely to experience disease progression ≤8 mths (38% v 24%). Reuse of platinum varied with time to progression; 37% at 0-5 mths; 76% at 6-8 mths; 94% at ≥9 mths. 174 centres (covering 1290 pts) had ≥1 progressions at 0-8 mths, 76 centres were classed low-use (<50% platinum 2nd line in 0-8mths) and 98 high-use.

The earlier progression of reference pts resulted in fewer getting 2nd line platinum at low use centres (41% v 56%), but not at high-use centres (76% v 77%). There was evidence of significantly shorter OS among reference pts at low-use centres (p=0.05, restricted mean survival 44.1 v 49.0 mths), but not at high-use centres (p=0.20, restricted mean survival 52.2 v 50.0 mths).

Conclusion

Improved OS with bevacizumab may result from an association with platinum-containing second line treatment: bev increases time to progression, increased time to progression increases the likelihood of second line platinum, second line platinum increases OS. It is possible therefore that OS might be improved by a lower time threshold for second line platinum chemotherapy, whether or not bevacizumab has been used.