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Original Article

Improved Survival from Ovarian Cancer in Patients Treated in Phase III Trial Active Cancer Centres in the UK

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Abstract

Aims: Ovarian cancer is the principal cause of gynaecological cancer death in developed countries, yet overall survival in the UK has been reported as being inferior to that in some Western countries. As there is a range of survival across the UK we hypothesised that in major regional centres, outcomes are equivalent to the best internationally.
Materials and methods: Data from patients treated in multicentre international and UK-based trials were obtained from three regional cancer centres in the UK; Manchester, University College London and Leeds (MUL). The median progression-free survival (PFS) and overall survival were calculated for each trial and compared with the published trial data. Normalised median survival values and the respective 95% confidence intervals (ratio of pooled MUL data to trial median survival) were calculated to allow inter-trial survival comparisons. This strategy then allowed a comparison of median survival across the UK, in three regional UK centres and in international centres.
Results: The analysis showed that the trial-reported PFS was the same in the UK, in the MUL centres and in international centres for each of the trials included in the study. Overall survival was, however, 45% better in major regional centre-treated patients (95% confidence interval 9–73%) than the median overall survival reported in UK trials, whereas the median overall survival in MUL centres equated with that achieved in international centres.
Conclusion: The data suggest that international survival statistics are achieved in UK regional cancer centres.

Key words: Cancer centre; clinical trial; ovarian cancer; prognosis; survival outcomes; UK

Introduction

Ovarian carcinoma is responsible for over 4000 deaths each year in the UK; more than all other gynaecological cancers combined. The standard treatment in the first-line setting is debulking surgery followed by cytotoxic chemotherapy with carboplatin and paclitaxel. Strategies to improve outcomes include the use of preoperative chemotherapy [1,2], dose-dense chemotherapy [3,4] or the addition of anti-angiogenic agents to standard doublet therapy [5–8].

In keeping with these advances, survival outcomes for ovarian cancer have improved worldwide, including in the UK. However, survival in the UK has been consistently reported to be worse than that in some other European countries, North America and Australia [9,10]. Within the UK there is evidence of variation in outcomes between

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cancer networks and regions [11,12]. This may be less related to socio-economic status [13] than to other prognostic factors at presentation. One critical issue is the quality of care, particularly after initial relapse, and to address this we collected ovarian cancer survival data from three UK cancer centres, which participated in five recent randomised trials in ovarian carcinoma. Our aim was to compare the progression-free survival (PFS) and overall survival statistics of women treated in regional cancer centres in the UK with those of women treated across the UK and internationally. We aimed to test the hypothesis that UK, major regional cancer centre-associated survival was superior to other UK centres.

Materials and Methods

Selection of Clinical Trials for Evaluation

Trials were selected if recently completed, overall survival statistics were available and the MUL centres had recruited sufficient numbers of patients to allow meaningful analysis. Five clinical trials met these criteria. The design and statistical plan for each trial have been described in the primary publications. Three trials involved patients receiving first-line treatment for ovarian cancer: CHORUS [2], GOG-0182-ICON5 [14] and ICON7 [6,7]. Two were in recurrent disease: ICON6 [8] and SaPPrOC [15], which recruited patients with platinum-sensitive and platinum-resistant disease, respectively.

The numbers of UK women recruited to each of the trials is presented as the numerator and the total number in the trial as the denominator: ICON5 363/4312 (8.4%); ICON7 375/1528 (24.5%); ICON6 379/486 (78%); SAPPROC 107/107 (100%); CHORUS 539/552 (97.6%). Trials were categorised as having been predominantly UK based (ICON6, CHORUS and SAPPROC) or international (ICON5 and ICON7). Thus, of the international group of trials, the UK contribution was 12.6% and in the UK-centric group of trials the contribution was 89.5% of patients.

Comparison of Specialist Centres and Overall Study Populations

Data were extracted from clinical trial databases and supplemented with clinical records for patients treated in three major regional cancer centres in the UK with expertise in the management of women with gynaecological cancers and in clinical trials (The Christie NHS Foundation Trust, Manchester; University College London Hospitals NHS Foundation Trust, London; and the St James's Institute of Oncology, Leeds: MUL).

Pre-treatment characteristics including FIGO stage, surgical outcomes and post-progression therapy were compared with those of the relevant overall trial populations. No distinction was made between the arms to which the patients were randomised and thus survival data across trial arms were summated for comparative purposes. Kaplan–Meier analysis, calculated from the date of study entry to the last available follow-up censored in September 2014, was used to calculate the median PFS and overall survival for MUL patients. MUL median survival values were then compared with those in the overall trial populations, taken from published data.

The median PFS and overall survival data were summarised further by calculating the ratio between the MUL median PFS or overall survival value and the trial median PFS or overall survival value for each study, where the trial median PFS or overall survival for the UK-centric studies was defined as 1. In the first part of the analysis we compared MUL survival with the median survival for UK-centred studies. We then compared the MUL survival statistics with the median survival in international trials, enabling a comparison between the three groups. The 95% confidence interval ratios for the MUL subset median values were similarly calculated.

When summating ratios from trials together to allow a comparison between MUL, UK and international data, the numbers of MUL patients recruited to each trial were used to weight the calculated overall survival ratio so that trials where MUL centres recruited more patients had a greater effect on the overall calculated survival ratio. Thus, the summated mean overall survival ratio (Figure 1) was calculated as: the sum of the products of the MUL survival ratio for each trial and the number of patients recruited from MUL centres to that trial, divided by the total number of MUL patients.

The effect of post-progression (off-trial) treatment was assessed using a post-progression survival ratio, calculated from the difference between median PFS and overall survival between MUL and overall trial populations.

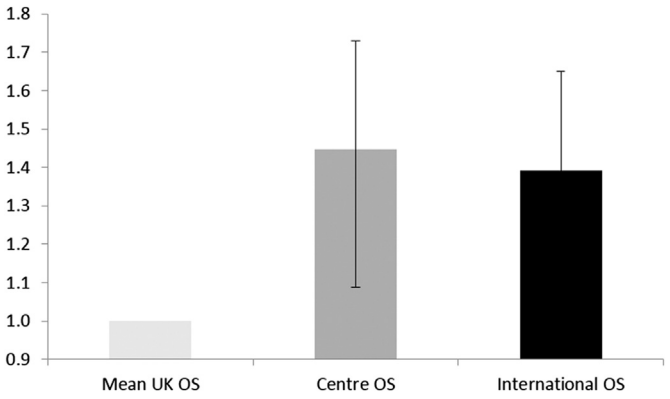

Fig 1. Overall survival in specialist cancer centres, international centres and the UK average survival. The data show the relative overall survival for patients treated in UK-centric trials, defined as unity and labelled as Mean UK OS. The Manchester, UCL and Leeds (MUL) centre overall survival is labelled as Centre OS, showing a 45% increase in overall survival in centre-treated patients, when compared with Mean UK OS. This is compared with the overall survival achieved by the MUL group in international clinical trials (the International OS bar). The International OS bar reflects the relative survival of MUL patients to the median overall survival of the international trial set compared with the UK OS, which is defined as 1. The MUL centre overall survival statistic is presented as ± 95% confidence intervals.

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