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What proportion of patients with stage 3 ovarian cancer are potentially cured following intraperitoneal chemotherapy? Analysis of the long term (10 years) survivors in NRG/GOG randomized clinical trials of intraperitoneal and intravenous chemotherapy in stage III ovarian cancer

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Provision of materials or patients: JKC;DKA;MM;TJH;BJM;FB;AAS;AB;PGR;KST;SSL;MAG;LJC;RSM.

Analysis and interpretation of data: JJJ;MF;JKC;OP.

Manuscript writing:OP;MF.

Critical review of the manuscript: All authors contributed.

Final approval of manuscript: All authors contributed.

Declaration of Competing Interest

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ygyno.2022.07.004>.

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Abstract

Objective.—Patients with advanced epithelial ovarian cancer (EOC) alive without progression at a landmark time-point of 10 years from diagnosis are likely cured. We report the proportion of patients with Stage III EOC who were long-term disease-free survivors (LTDFS 10 years) following either intraperitoneal (IP) or intravenous (IV) chemotherapy as well as the predictors of LTDFS.

Methods.—Data from 3 mature NRG/GOG trials (104, 114, 172) were analyzed and included demographics, clinicopathologic details, route of administration, and survival outcomes of patients living 10 years assessed according to the Kaplan-Meier method. Cox regression survival analysis was performed to evaluate independent prognostic predictors of LTDFS.

Results.—Of 1174 patients randomized, 10-year overall survival (OS) was 26% (95% CI, 23–28%) and LTDFS 10 years was 18% (95% CI, 16–20%). Patients with LTDFS 10 years had a median age of 54.6 years ($p < 0.001$). Younger age ($p < 0.001$) was the only independent prognostic factor for LTDFS 10 years on multivariate Cox analysis.

Conclusions.—Approximately 18% of patients were LTDFS 10 years. They form the tail end of the survival curve and are likely cured. Our results provide a comparative benchmark to evaluate the impact of PARP inhibitors in 1st line maintenance trials on survival outcomes.

Keywords

Advanced ovarian cancer

1. Introduction

Patients with advanced stage epithelial ovarian cancer (EOC) who survive beyond 10 years from initial diagnosis without recurrence have a life expectancy that is similar to that of an age-matched population of women without ovarian cancer and may be considered cured [1]. Registry studies report 10-year survival figures of 13% - 25% among patients with stage III and IV EOC with most of the 10-year survivors having stage III disease [2–4]. These 10-year survivors comprise a heterogeneous group of patients and include a subgroup who remain disease free after initial treatment and are likely cured as well as patients living with recurrent disease who may have had multiple lines of treatment. In most reports and studies reporting long term survivors (LTS) these two distinct groups of patients are considered together and there is a paucity of data on the proportion of patients who are alive and disease free and likely cured as compared to the overall number of patients living with recurrent disease. The large registry studies do not provide this important information and very few, if any trials with long term follow up have reported on the patients at the tail of the survival curves either, and typically only report median overall survival (OS).

There have been significant improvements in the median OS of patients with advanced stage EOC over the last 30 years. However, due to the non-proportional hazards in advanced EOC, improvements in median survival, while important, do not necessarily lead to an increase in the number of patients who are LTS > 10 years. Although, the 5-year case fatality rates in women with EOC have fallen significantly over the last 30 years, the 12-year case fatality rates have only decreased by 1.2% suggesting that the improvements in 5 year survival has not significantly impacted on long term ovarian cancer specific mortality [5]. The number of patients who are long term overall survivors (LTOS) > 10 years appears to be a constant over the last 20–30 years since the introduction of platinum-based chemotherapy despite more aggressive surgery and a wide range of treatments that have been investigated in clinical trials [3]. For example, Thigpen et al [6] reported 10 year survival ranging from 10 to 20% in early generation GOG trials that included platinum based chemotherapy trials in the 1980's which is not appreciably different to more recent reports [2,6]. Most clinical trials report on 5-year survival, and those with longer follow up on the median survival, which is the time when 50% of patients have died, but very few report on 10-year survival and the tail end of the Kaplan-Meier survival curve. Median OS is commonly used as an end point for efficacy as it allows timely reporting of the results of trials but the proportion of patients alive without recurrence beyond the median is not often available. The tail end of patients the survival curve can provide information on patients that not only exceed the median survival, but include a proportion that might be considered cured [7], i.e. alive without disease recurrence. To the best of our knowledge no clinical trials or registry studies have reported on the proportion of patients with Stage III EOC who are disease free at 10 years and this is the focus of this report. This data assumes increased importance in the era of maintenance therapies with PARP inhibitors after 1st line chemotherapy as it provides a benchmark to evaluate their impact on LTDFS and whether there is a substantial increase in the proportion of patients who are cured with maintenance therapy following 1st line chemotherapy.

We chose to analyze patients with Stage III EOC who were enrolled in 3 NRG/GOG randomized trials of IP v IV chemotherapy [Supplementary Table 1] that have all been previously reported and which have long term follow up data available. The patients entered in these trials represent a more favorable subset of patients with advanced stage EOC in that they had adequate surgery and most had relatively small volume disease, a good performance status and were deemed suitable for inclusion in trials of IP chemotherapy. Furthermore, meta-analyses of IP vs IV chemotherapy in advanced ovarian cancer have reported that IP chemotherapy is associated with an increase in both progression free survival (PFS) and median OS but none of these trials have reported on the tail of the survival curve and whether there was an increase in the number of patients likely cured with IP vs IV chemotherapy.

SWOG 8501/GOG 104 [8] included 546 eligible patients (298 entered through GOG) enrolled between 1986 and 1992; 279 who were randomized to IV cisplatin and cyclophosphamide and 267 to IP cisplatin and IV cyclophosphamide at the same doses every 3 weeks for 6 cycles. They had a median follow-up of 13.8 years. The estimated median survival was significantly longer in the IP group (49 months; 95% CI 42–56) compared to the IV cisplatin arm (41 months 95% CI 34–47). The risk of death was lower in the IP group (HR 0.76; 95% CI 0.61–0.96; $P=0.02$).

In GOG 114 [9] 523 patients were enrolled of whom 462 were eligible for inclusion for analysis were randomized to receive either IV paclitaxel 135 mg/m² over 24 h followed by IV cisplatin 75 mg/m² every 3 weeks for six courses or IV carboplatin (area under curve 9) every 28 days for two courses, then IV paclitaxel 135 mg/m² over 24 h followed by IP cisplatin 100 mg/m² every 3 weeks for six courses. The median follow-up was 10 years. The increase on OS was of borderline statistical significance (median 63 vs 52 months; RR 0.81; $P=0.05$).

Finally, GOG 172 [10] randomized 429 patients with no residual mass >1.0 cm to receive 135 mg of intravenous paclitaxel per m² over a 24-h period followed by either 75 mg of intravenous cisplatin per square meter on day 2 (intravenous-therapy group) or 100 mg of intraperitoneal cisplatin per square meter on day 2 and 60 mg of intraperitoneal paclitaxel per square meter on day 8 (intraperitoneal-therapy group) every three weeks for six cycles. The median follow-up was 10.7 years. Median survival with IP therapy was 61.8 months (95% CI, 55.5 to 69.5), compared with 51.4 months (95% CI, 46.0 to 58.2) for intravenous therapy (adjusted hazard ratio, 0.77; 95% CI, 0.65 to 0.90; $P=0.002$) [11].

The data from patients enrolled in these studies was combined and the proportion of LTS assessed, and of particular interest was the proportion of patients who are disease free at this time point as this represents a unique group of patients who are likely cured.

2. Methods

2.1. Patients

The data set included patients from GOG-104, 114, and 172 with optimally debulked stage III epithelial ovarian or primary peritoneal cancer. The data collected included patient

demographics, clinicopathologic information, chemotherapy administration, and survival outcomes.

The consort diagram [Fig. 1] shows a combined 1174 eligible patients from the 3 studies (GOG-104, GOG-114 and GOG-172) randomized to IV or IP chemotherapy. 584 patients received IV chemotherapy and 590 IP chemotherapy. At 10-year follow-up in patients randomized to IV chemotherapy, 475 (81.3%) had died or were lost to follow-up, 25 (25/584; 4.3%) were alive but with disease recurrence and 84 patients (84/584; 14.4%) were LTDFS 10 years. Of the 590 patients that received IP chemotherapy, 478 (81%) had died or were lost to follow up at 10 years, 36 (36/590; 6%) were alive but had disease recurrence, and 76 patients (76/590; 12.9%) were LTDFS 10 years.

2.2. Statistical analysis

PFS and OS were modelled as a function of baseline clinical covariates to measure their association. Categorical variables were compared between the patient subgroups by the Pearson chi-square test and continuous variables by the Wilcoxon–Mann–Whitney test. Survival was estimated using the Kaplan–Meier method. Using a landmark approach at 10 years, Cox regression survival analysis was performed to evaluate independent prognostic factors that may predict LTDFS at 10 years. These were PFS 10 years, age, race (non-white v white), histology (other v serous), performance status (1 v 0; and 2/3 v 0), gross residual disease, and mode of chemotherapy (IV v IP). Multicollinearity was checked through the method of variance inflation factors (VIF) and found unproblematic. All statistical tests were two-tailed with the significance level set at $\alpha = 0.05$. Statistical analyses were performed using the R programming language and environment.

3. Results

The number of patients enrolled and analyzed, including their long-term survival outcomes, are summarised in the CONSORT diagram [Fig. 1]. Demographics and clinicopathological characteristics are outlined in Table 1. Median age across the three studies was 57.2 years, patients were predominantly white (78%) with serous histology (68.4%) and performance status of 0–1 (94%).

The median follow-up time for all patients was 141 months (95% CI: 137–157mo). Of 1174 patients eligible for analysis, 18.8% (221/1174) were alive at 10 years, which included 13.6% ($n = 160$) LTDFS at 10 years and 5.2% ($n = 61$) alive with recurrent disease. Kaplan–Meier estimates demonstrated a LTOS 10 years of 26% (95% CI, 23–28%) and LTDFS at 10 years of 18% (95% CI, 16–20%) [Fig. 2].

The patients who were LTDFS 10 years had a median age of 54.6 years, with serous histology reported in 63.7% (102/160), 56.2% (90/160) with evidence of gross residual disease, and tumors with good-differentiation in 13.1% (21/160), moderate differentiation in 25.0% (40/160) and poor differentiation in 26.2% (42/160) [Supplementary Table 2]. Statistically significant differences were seen between the LTDFS 10 years, LTOS 10 years who had recurrence and deceased/censored with respect to age, histology, tumor grade and presence of gross residual disease. Patients who are LTOS 10 and LTDFS 10 were

younger ($p < 0.001$) with a median age of 54.4 years and 54.6 years respectively compared to patients who died or censored who had a median age of 58.1. Good tumor grade was present in only 7.0% patients compared to 19.7% and 13.1% in the LTS respectively ($p < 0.001$). A higher proportion of patients who died had gross residual disease 68.8% v 55.7%/56.2% ($p = 0.001$). There were no statistically significant differences between the LTDFS 10 years and the rest of the patient population in terms of histology ($p = 0.133$), race ($p = 0.605$), performance status ($p = 0.535$), or receipt of intraperitoneal or intravenous chemotherapy ($p = 0.307$).

Multivariate Cox analysis of PFS and OS [Table 2] of patients who were disease free at 10 years showed that younger age was the only independent prognostic factor for LTDFS 10 years (HR = 1.076; 95% CI, 1.03–1.12; $p < 0.001$) and LT(DF)OS 10 years (HR = 1.097; 95% CI, 1.042–1.155; $p < 0.001$). Other characteristics analyzed included race, histology, performance status (1 compared to 0; and 2/3 compared to 0), tumor grade, absence of gross residual disease and type of chemotherapy (IV v IP).

Overall survival analysis at 10 years of patients who were disease-free compared to those who had recurrent disease [Table 3], showed that patients with a longer disease-free interval have a lower risk of death (HR 0.225; 95% CI, 0.118–0.429; $p < 0.001$). Age at study entry was prognostic of survival, with older patients at a higher risk of relapse or death (HR 1.047; 95% CI, 1.017–1.077; $p = 0.002$).

4. Discussion

In patients with Stage III EOC who were included in 3 mature NRG/GOG trials of IV v IP chemotherapy, 18% were LTDFS at 10 years. After adjusting for known prognostic factors, long term survival was associated with younger age, but not with histology, performance status, presence of residual disease or mode of administration of chemotherapy. There was also no association with race, however, it should be noted that these studies included predominantly white patients (77.5%). Lack of racial and ethnic diversity has been recognised as a deficiency of cancer clinical trials [12]. LTDFS 10 years represents the proportion of patients who are likely cured and had an exceptional response to first line treatment in a relatively favorable subset of patients with Stage III ovarian cancer who had optimal debulking (based on definitions of optimal cytoreduction at the time of the trials) and met the eligibility criteria for inclusion in IP vs IV chemotherapy clinical trials. The LTDFS 10 years is likely lower in an unselected real-world population of patients with advanced stage ovarian cancer. LTDFS 10 years should be included as an endpoint in clinical trials in addition to median OS as overall cure, although uncommon, remains the ultimate aim of treatment [2].

Relative survival is a summary statistic which accommodates for other causes of death and is defined by the National Cancer Institute Surveillance, Epidemiology, and End Results (SEER) group as a “ratio of proportion of observed survivors in a cohort of cancer patients to the proportion of expected survivors in a comparable set of cancer free individuals.” A Swedish population-based study demonstrated the relative survival rate for EOC declined from 46.2% at 5 years to 38.4% at 10 years (95% CI, 34.5%–42.8%), with a median survival

of 4.5 years (95% CI, 3.9–5.5 years). A Californian Cancer Registry retrospective study showed 31% OS beyond 10 years in 5173 patients with EOC combining all stages [13], with 980/5173 (18.9%) Stage III patients. Analysis of 40,692 patients from the SEER database reported relative survival of Stage III EOC patients to be 36% at 5 years and 23% at 10 years [2]. These figures are similar to our findings but do not distinguish between the proportion alive without recurrence and those living with recurrent EOC. The SEER registry data also shows that although 80% of ovarian cancer deaths occur within 5 years of diagnosis, almost 50% of patients who are alive at 5 years will die after this with the majority of deaths due to ovarian cancer [2,14]. Even among patients who are progression free at 5 years, late relapse may occur, and we observed disease recurrence between 5 and 10 years in 53 patients in our study, thus supporting the need for follow up beyond 5 years [14].

In this analysis our aim was to determine the patients with LTDFS 10 years in each of the 3 NRG/GOG trials of IV v IP chemotherapy. The rationale for using IP chemotherapy in EOC is based on its known patterns of spread within the intraperitoneal cavity and the pharmaco-kinetic advantage of intraperitoneal cisplatin over IV administration, with analysis of results from GOG 114 and 172 reporting an increased median OS by 10.4 months in favor of IP chemotherapy at a median follow up of 10.7 years (61.8 months v 51.4 months) [11]. A major advantage in pooling results from these 3 mature trials is a large cohort of patients with extended follow up data at a landmark of 10 years. However, as a retrospective analysis we are limited by the heterogeneity of drug regimens and scheduling used in each study, such as incorporation of paclitaxel into GOG 114 and 172 but not 104. This is a selective group of patients who were deemed fit for inclusion in a clinical trial, which may not reflect real world populations with EOC. The details on the impact on survival due to deaths from competing causes should be balanced between the arms but did not form part of our analysis.

In patients with newly diagnosed advanced EOC, there is an initial decline in survival from 0 to 5 years from diagnosis, and a further, but less steep decline in survival from 5 to 10 years [2]. A proportion of the patients that survive to 10 years have received multiple subsequent lines of treatment following 1st recurrence. Patients treated for EOC who are disease free beyond 10 years have been reported to have the same mortality as an age matched population [1] so it is important to differentiate between long-term survivors who are alive with recurrent disease after multiple lines of treatment from the subset who are alive without evidence of disease recurrence. They are clearly very different and should be reported as separate entities rather than combined. The proportion of patients who are alive and disease free as reported by the LTDFS 10 is a relevant endpoint, not just to report in clinical trials but also to discuss with patients.

Median OS is an important endpoint in clinical trials and includes a mix of patients alive with and without recurrent disease at a specific time point. The median provides a measure of when 50% of patients have died by that time point, with little known about the patients at the tail end of the survival curve who are alive beyond the median, which may also include a proportion of patients alive without disease progression [7]. In order to represent this tail end of the survival curve better, alternative metrics such as mean OS which is calculated from the area under the Kaplan-Meier curve, cure fraction which is the proportion of patients who assume a similar mortality to age matched population, or landmark survival rates such as 5

or 10 years have been suggested [7]. Taking into account the disease tempo of patients with EOC, survival >10 years can be used to define long-term survival, as mortality rate beyond that time point is similar to an age matched population [1]. Although survival at 10 years may not necessarily equate with cure given the figures include an unknown proportion of patients living with recurrent disease who are unlikely to be cured. However, there are an increased number of patients with recurrent ovarian cancer—so called exceptional responders to PARP inhibitors who are alive and progression free beyond 5 years although we don't have 10-year survival data available [15].

Several clinicopathologic characteristics have been shown to be associated with long term survival in patients with EOC. This includes younger age [4,16,17], early stage, low-grade tumors, histology [16], optimal cytoreduction [4,17,18], use of intraperitoneal chemotherapy [5], complete response to primary treatment [19], molecular signature [20,21] and good performance status¹⁸. The studies are heterogeneous, with some studies showing positive results for only one or two factors. The only independent prognostic factor we identified for LTDFS 10 years was younger age at diagnosis. The role of age may be due to impact of comorbidities, or different tumor biology including higher probability of BRCA mutations in younger patients. The percentage of patients who were LTDFS 10 years in our analysis (18%) was identical to another study reported by Rose et al [22] which combined the data from 8 GOG trials (GOG-111, 114, 132, 152, 158, 162, 172, and 182), and included patients with optimal and suboptimally debulked stage III and stage IV EOC. The aim of this study was to analyze clinical prognostic factors for survival after recurrence and they excluded 18% (1343/7651) patients from the analyses as they were disease free without recurrence. They included patients with optimal as well as suboptimal residual disease but median follow-up time was not reported as long term disease free survival was not the primary aim of Rose's study. The finding that 18% of patients with advanced EOC who were recurrence free after long follow up is remarkably consistent with our study that close to 20% of patients with advanced EOC are exceptional responders and likely cured. Unlike previous reports, we did not find an association with optimal debulking, mode of administration of chemotherapy, race, histology or performance status with LTDFS 10 years. A multicenter US study which identified 203,10-year survivors of HGSOE encompassing all stages reported 88/203 (46.8%) of the long-term survivors were recurrence free after first line treatment, with optimal cytoreduction (defined as <1 cm residual disease) identified as a prognostic factor [17]. These patients had not recurred after initial treatment and similar to our subset of patients could be considered cured, while the remainder of long term survivors were alive with recurrence underscoring the importance of differentiating between these two subsets when reporting long term survival.

Poor prognostic factors can be present in patients who are LTS after first line treatment, as demonstrated in the Cress et al [13] study which included over one-third advanced stage, high grade morphology, or patients with serous histology in their LTS cohort, suggesting exquisite chemosensitivity or immunological differences [13]. In our analysis, 18.9% of patients who were LTDFS 10 years were classified as having good-differentiation based on definitions at the time of the original GOG studies, and it is possible that a proportion of these would be classified as low grade serous cancers based on the current definition. Some of the prognostic markers that have been explored include tumor infiltrating lymphocytes

(TILs) and somatic mutations. Density of CD3 and CD103 expressing intraepithelial TILs in HGSOC has been shown to correlate with survival [23,24], with longer OS seen when both are expressed in high levels [24]. Differential expression of three genes, CYP4B1, CEPT1 and CHMP4A [25] was observed in patients who had no disease recurrence compared to those who were alive but living with disease recurrence. Many other studies have explored prognostic variables, but have been heterogeneous in their methodology with utilization of different gene arrays, small sample sizes, and reported various sets of prognostic genes [26,27]. The introduction of genomic analysis in the treatment of patients with EOC has led to a tailored approach with the incorporation of PARP inhibitors in patients with BRCA and other HRD gene mutations with improved outcomes. Although Kotsopoulos [28] reported that BRCA mutation status had no impact on long term survival, there have been other studies which have shown the presence of a *BRCA2* mutation is independently associated with OS [29,30]. As these studies were performed in the pre-PARP inhibitor era, the overall impact of maintenance PARP inhibitors on long-term survival will be ascertained with longer follow up. An important limitation of our analysis is that germline BRCA status was not available on a large portion of the patients included in our analyses. Nonetheless, our results can be used as a benchmark to compare against LTDFS data from studies conducted after the adoption of maintenance therapies such as with PARP inhibitors after 1st line chemotherapy. Further work needs to be done to elucidate the molecular, genetic and/or clinical characteristics of these patients who are exceptional responders and remain disease free 10 years from diagnosis after first line treatment. LTDFS at 10 years should also be included as an endpoint in clinical trials. This underscores the importance of embedding translational research including collection of tumor and blood from patients entered in clinical trials in advanced EOC.

5. Conclusions

Analysis of survival in 3 NRG/GOG studies at the landmark time-point of 10 years showed 26% LTOS 10 years and 18% LTDFS 10 years. Younger age at diagnosis was the only independent prognostic factor. The proportion of patients who are LTDFS 10 years are likely cured. Our results can be used as a benchmark to compare with the impact of newer treatment strategies such as maintenance PARP inhibitors after first line chemotherapy on long term survival. Further work is needed to understand the predictors of exceptional responders and whether the long-term disease-free survivors can be identified at initial diagnosis.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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HIGHLIGHTS

- Long term survivors with advanced ovarian cancer are uncommon and include patients alive with or without disease recurrence
- Clinical trials don't report the patients who are long term disease free survivors (LTDFS 10 years) and likely cured
- Almost 20% of patients were LTDFS 10 years in GOG trials of intravenous vs intraperitoneal chemotherapy
- Apart from younger patient age at diagnosis there were no other factors associated with LTDFS 10 years

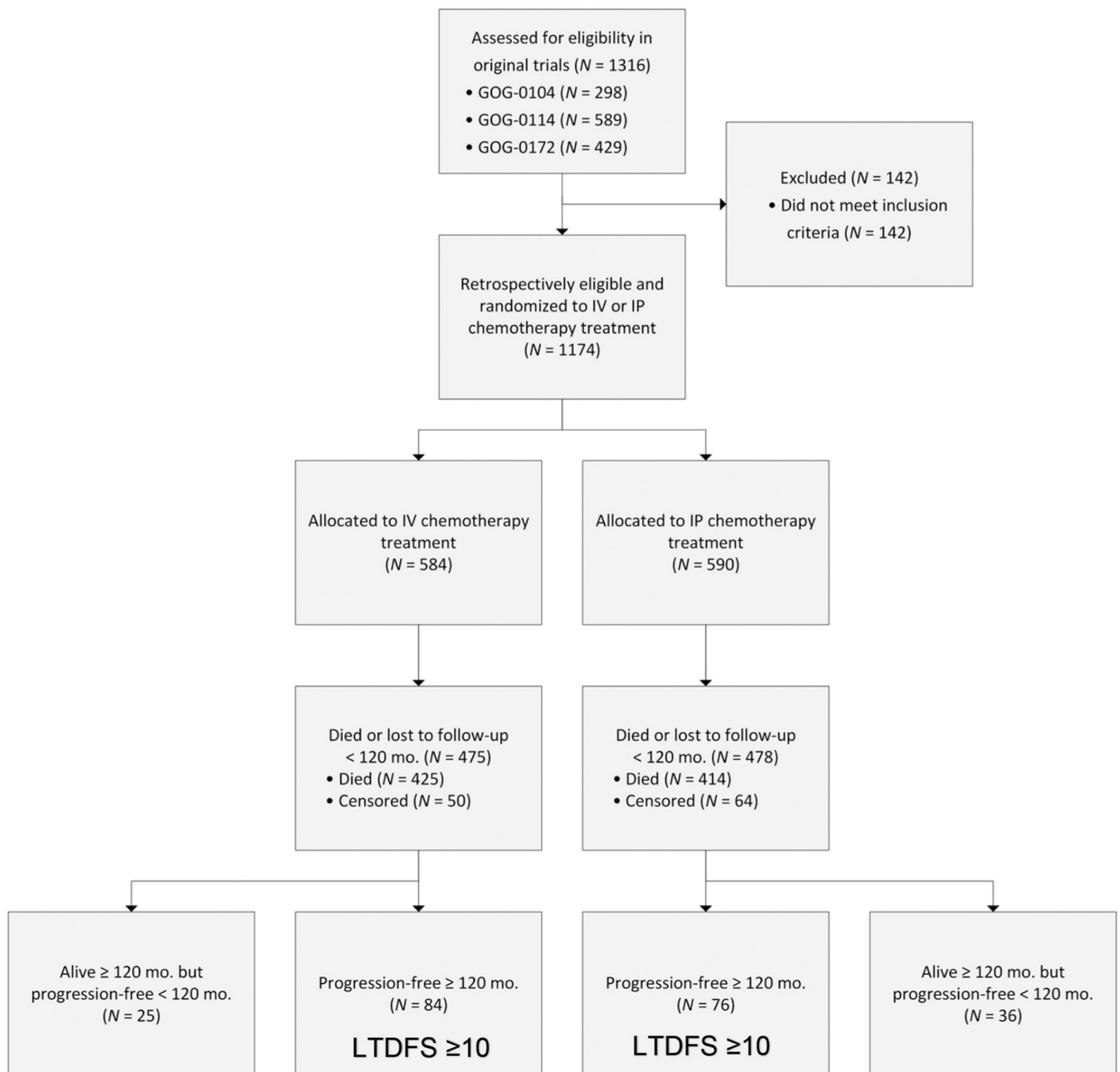


Fig. 1. Consort diagram of patients entered into GOG 104, 114 and 172 randomized to IP vs IV chemotherapy. Of 1174 patients in these 3 trials, 221 (18.8%) were reported to be alive 10 years from initial diagnosis and 160 (13.6%) were LTDFS 10 years and had not recurred.

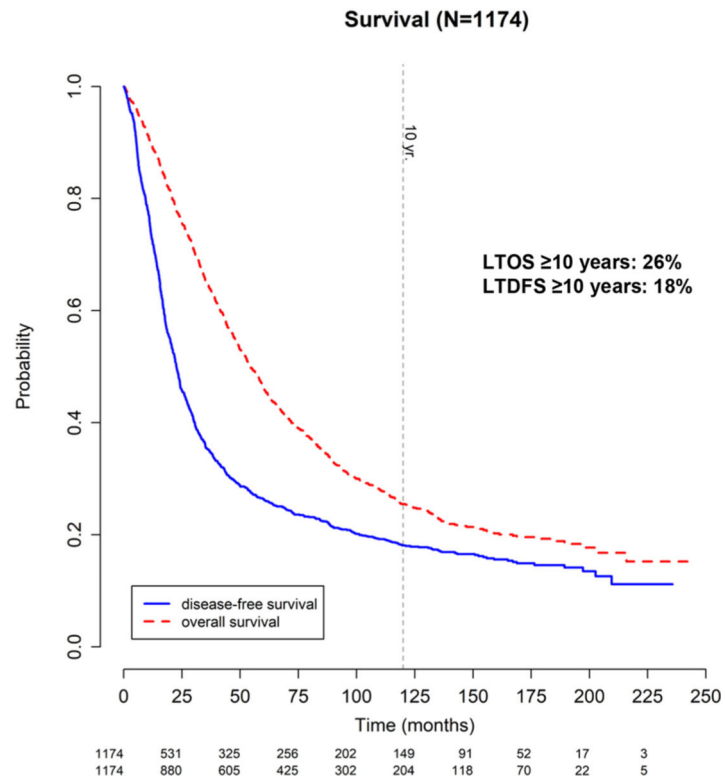


Fig. 2. Kaplan-Meier curve showing long-term overall survival (LTOS) 10 years and disease-free survival (LTDFS) 10 years.

Table 1

Baseline patient demographics and clinical characteristics.

	N
Age years	1174 48.6 57.2 65.6
Race/ethnicity	1174
White	77.5% (910)
Black	4.1% (48)
Hispanic	2.6% (31)
Asian	1.6% (19)
Other	14.1% (166)
Histology	1174
Serous	68.7% (807)
Clear-cell	3.9% (48)
Endometrioid	9.1% (107)
Mucinous	2.1% (25)
Mixed epithelial	6.0% (71)
Other	10.1% (118)
FIGO stage	1174
III	100% (1174)
Tumor grade (differentiation)	876
Good	8.5% (100)
Moderate	28.6% (336)
Not graded	1.2% (14)
Poor	36.3% (426)
NA	25.4% (298)
Performance status	1174
0	58.3% (685)
1	35.7% (419)
2/3	6.0% (70)
Gross residual disease	1174
Yes	66.4% (780)
No	33.6% (394)
Regimen	1174
IP	50.3% (590)
IV	49.7% (584)
Treatment	1174
Cisplatin + cyclophosphamide	12.6% (148)
Cisplatin (IP) + cyclophosphamide	12.8% (150)
Cisplatin + paclitaxel	37.1% (436)
Cisplatin (IP) + paclitaxel	17.4% (204)
Cisplatin (IP) + carboplatin + paclitaxel	20.1% (236)
GOG Protocol	1174

	N
GOG-0104	25.4% (298)
GOG-0114	39.4% (462)
GOG-0172	35.3% (414)
Status at 120 mo.	1174
Died or censored <10 years	81.2% (953)
LTOS 10 years with recurrence	5.2% (61)
LTDFS 10 years	13.6% (160)

Table 1 shows the demographics and clinical details of the patients from GOG-104, 114 and 172.

a b c represent the lower quartile *a*, the median *b*, and the upper quartile *c* for continuous variables.

N is the number of non-missing values. NA – not available.

Numbers after percentages are frequencies.

Multivariate progression-free survival and overall survival analysis of patients disease-free 10 years.

Table 2

Characteristic	PFS			OS		
	HR	95% CI	p-value	HR	95% CI	p-value
Age	1.076	1.030–1.123	< 0.001	1.097	1.042–1.155	< 0.001
Race (non-white v white)	1.248	0.447–3.481	0.673	1.747	0.576–5.301	0.325
Histology (other v serous)	0.670	0.271–1.660	0.387	0.746	0.284–1.957	0.551
Performance status (1 v 0)	0.633	0.123–3.263	0.585	0.727	0.099–5.330	0.754
Performance status (2/3 v 0)	2.065	0.202–21.108	0.541	4.162	0.334–51.843	0.268
Gross residual disease	0.659	0.205–2.119	0.484	0.635	0.189–2.132	0.463
Mode of chemotherapy (IV v IP)	0.707	0.281–1.776	0.460	0.654	0.235–1.819	0.415

Multivariate Cox analysis of baseline clinical covariates and effect on the PFS and OS of patients disease-free 10 years. The hazard ratio, confidence interval and p-value are presented for each characteristic assessed

Table 3

Multivariate overall survival analysis of patients who survived 10 years.

Characteristic	HR	95% CI	p-value
PFS 10 years	0.225	0.118–0.429	< 0.001
Age	1.047	1.017–1.077	0.002
Race (non-white v white)	1.160	0.517–2.606	0.719
Histology (other v serous)	1.029	0.532–1.992	0.933
Performance status (1 v 0)	0.871	0.339–2.235	0.773
Performance status (2/3v0)	2.591	0.766–8.759	0.126
Gross residual disease	1.302	0.628–2.699	0.478
Mode of chemotherapy (IV v IP)	0.728	0.383–1.384	0.332

Multivariate Cox analysis of overall survival for all patients who lived 10 years after study entry, comparing the patients who were LTDFS 10 years and those who were alive at 10 years but had recurrent disease. The hazard ratio, confidence interval and p-value is presented for each characteristic assessed.

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