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THE POWER OF SHARED PURPOSE: Transforming Gynecologic Cancer Care

Randomized phase II trial of weekly ixabepilone ± biweekly bevacizumab for platinum-resistant or refractory ovarian / fallopian tube / primary peritoneal cancer (NCT03093155): updated survival and subgroup analyses

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INTRODUCTION

The microtubule-stabilizing agent, ixabepilone, may retain activity in paclitaxel-resistant disease. We previously reported* the efficacy/safety of weekly ixabepilone ± biweekly bevacizumab in chemotherapy-resistant ovarian cancers. The study met its primary and secondary endpoints with an improvement in progression-free (PFS) and overall survival (OS), with no new safety signals. Analyses were originally performed in 11/2020. We now describe updated best objective response rates (ORR), PFS and OS in a mature data set. Additional subset analyses were performed.

METHODS

Patients with platinum-resistant/-refractory ovarian cancer were stratified by prior bevacizumab treatment and randomized to receive weekly ixabepilone 20 mg/m^2 days 1,8,15 ± biweekly bevacizumab 10 mg/kg days 1, 15 of a 28-day cycle as part of a multi-site prospective randomized trial. Survival was analyzed using the Kaplan-Meier method with one-sided log-rank tests and Cox regression. Two-sided Fisher's exact tests were used to compare response rates. Subgroup analyses were illustrated using Forest plots and analyzed with 2-tailed Wald tests. Patients were considered 'taxane-resistant' if they had demonstrated disease progression within 6 months of paclitaxel/docetaxel administration and 'taxane-refractory' if they progressed while receiving a taxane or demonstrated persistence of disease on end-of treatment assessment that prompted initiation of a new line of therapy. All others were deemed 'taxane-sensitive.'

RESULTS

A total of 37 patients were randomized to monotherapy (IXA) and 39 patients to combination therapy (IXA + BEV). In both groups, patients received a median of 4 prior lines. The groups did not differ by taxane-free interval. At the data cutoff (03/29/2023), 75 PFS events and 70 deaths had occurred among 76 participants. A dose reduction of 20% was necessary in 59% (IXA) and 64% (IXA+BEV) of participants, but even 2 dose reductions did not necessarily diminish PFS or OS benefit **[Figure 1-top]**. ORR were higher in the IXA+BEV arm (38.4% vs 8.1%, p=0.003). Median PFS was 5.5 versus 2.2 months, HR 0.31, 90%CI 0.20-0.49, p<0.001). Median OS was 10.3 versus 6.0 months (mo) (HR 0.56, 90%CI 0.38-0.84, p=0.02). Among the IXA and IXA+BEV arms, most patients were paclitaxel-refractory/-resistant (51% [n=19] and 67% [n=26], respectively). The addition of BEV to IXA conferred benefit in PFS (HR 0.31, 90%CI 0.20-0.48, p<0.001) and OS (HR 0.59, 90%CI 0.39-0.88, p<0.03) even when adjusting for prior taxane response. There were no complete responses, but in the combination arm, 14 patients achieved a durable response (stable disease or partial response > 6 months) **[Figure 1-bottom]**.

In heavily pre-treated ovarian cancers, **ixabepilone and bevacizumab** achieves an **ORR of 38%**

The combination significantly **improves PFS** (5.5 mo) **& OS** (10.3 mo) compared to ixabepilone alone regardless of prior taxane response and dose reductions

FIGURE 1- top

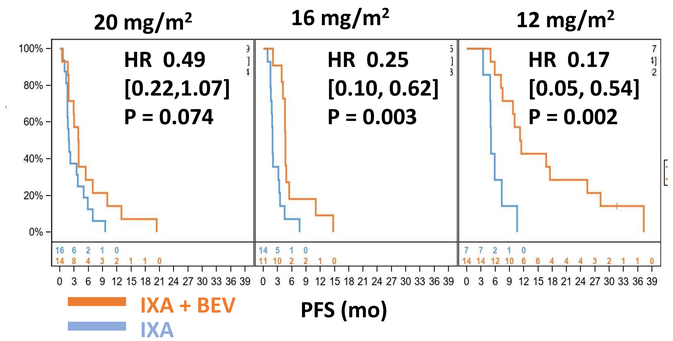
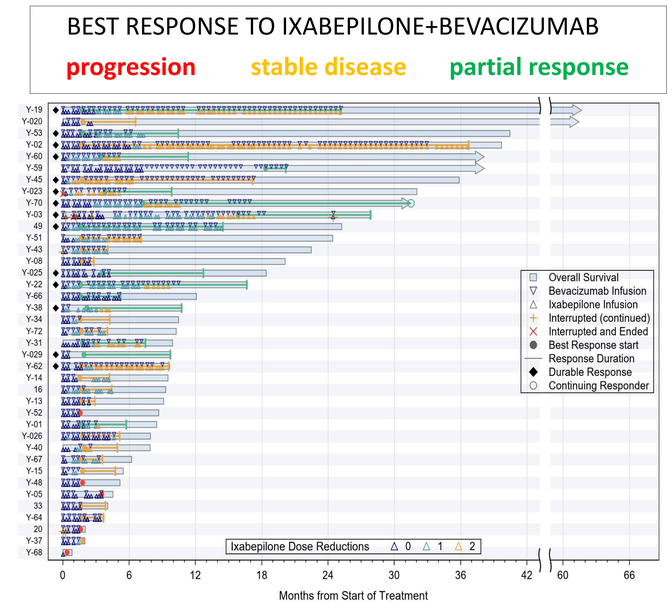


FIGURE 1- bottom



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* Roque DM, Siegel ER, Buza N, et al. Randomised phase II trial of weekly ixabepilone ± biweekly bevacizumab for platinum-resistant or refractory ovarian/fallopian tube/primary peritoneal cancer. *Br J Cancer* 2022; 126(12):1695-1703.doi: 10.1038/s41416-022-01717-6 c