The impact of tumor molecular profile-directed treatment on survival in ovarian cancer

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Updated abstract

The weight in absolute advantage tumor molecular profile-directed treatment in ovarian, primary peritoneal and fallopian tube cancer.

Methods

The Caris Registry™, approved by Caris Life Sciences® (Caris), contains the Caris® Registry®, a database of histopathological and molecular variables for patients who received molecular profiling. The registry was created to provide research-grade data, which is used to study agents of degree of potential therapeutic benefit. The Caris® Registry™ was operated for all patients with a diagnosis of ovarian, primary peritoneal, and fallopian tube cancer who underwent comprehensive molecular characterization of their tumors. Treatment profile-directed treatment in ovarian cancer was then performed. This subgroup analysis excluded 60 patients from the Analysis Population of 348, reducing the Benefit cohort to 140 and the Lack of Benefit cohort to 168. The median overall survival from the time of profiling performed for patients included in the Benefit cohort has not yet been reached but was significantly longer than patients included in the Lack of Benefit cohort who lived for a median of 32.6 months after profiling (HR 0.54, 95% CI 0.37-0.80; p<0.001).

Background

A 5-year study showed that comprehensive molecular profiling identified molecular targets in patients with refractory, metasta- 
sed diseases, including patients who had failed prior systemic treatments. The data was obtained through Caris Life Sciences’ Molecular Intelligence™ (CMI™) platform, an FDA-cleared in vitro diagnostic (IVD) used to identify patient-specific molecular targets. The Caris Registry™ was established as a post-marketing registry to offer an ongoing oncology molecular profiling-based clinical outcomes database.

Methods

Tumor biopsy samples were analyzed with a combination of Sanger sequencing, next generation sequencing, pyrosequencing, immunohistochemistry (IHC), gene amplification with fluorescent/chromogenic in-situ hybridization (F/C-ISH), and ribonucleic acid (RNA) analysis. Tissue samples were sequenced at Caris Life Sciences® using a Cancer Hotspot panel.

Statistical considerations and patient cohort selection

Of the 348 patients enrolled, 316 patients were evaluable and comprised the Analysis Population (n=316). Of the 316 patients, 170 were classified in the Benefit cohort and 146 were classified in the Lack of Benefit cohort. The analysis population (n=316) was divided into two cohorts based on whether the treatment at least was associated with potential lack of benefit or any true benefit of following diagnosis.

Demographics

Potential benefit and no treatments associated with lack of benefit while the "Lack of Benefit" cohort received at least one agent with death/censoring using the Kaplan-Meier method.

Evaluation of the effectiveness of Caris Life Sciences® Molecular Intelligence™ (CMI™) directed therapy, the Caris Registry™ was performed. A review of all patients treated in a single center in Australia resulted in clinical and survival benefits in over half of the patients. The impact of tumor molecular profile-directed treatment on survival in ovarian cancer.

Benefit of some profiling-directed agents by cohort

The table below shows select treatments associated with benefit with each lack of benefit according to the results of the DNA’s reports. More of the patients included in the Benefit cohort were predicted to have platinum and taxane resistance and may have received these treatments in an unplanned manner in line with standard care guidelines.

Overall survival from time of diagnosis

Median overall survival observed for patients included in the benefit cohort (158.0 months) compared to patients included in the Lack of Benefit cohort (43.4 months) treated towards significance (HR 0.54, 95% CI 0.37-0.80; p<0.001). Patients referred to Caris Life Sciences® between 2009 and March 2014 were enrolled in the Caris Registry™.

Post-profiling survival sub-analysis

A subgroup analysis of the patients who had received at least one post-profiling treatment was performed. This subgroup analysis excluded 60 patients from the Analysis Population of 348, reducing the Benefit cohort to 140 and the Lack of Benefit cohort to 168. No patients who received agents associated with lack of benefit in the Benefit cohort has not yet been reached but was significantly longer than patients included in the Lack of Benefit cohort who lived for a median of 32.6 months after profiling (HR 0.54, 95% CI 0.37-0.80; p<0.001).

References


Demographics

- Patient characteristics (age, race, stage at diagnosis, and site of biopsy analyzed) were well balanced between the Benefit and Lack of Benefit cohort.
- Of the 348 eligible and evaluable patients, 303 were diagnosed with epithelial ovarian carcinoma, 26 with primary peritoneal carcinomas and 19 patients with fallopian tube carcinoma.
- The distribution of primary site of disease was similar between the two cohorts.
- There was significant difference in the distribution of histology between the two cohorts. Patients in the Benefit cohort experienced significantly longer post-profiling survival in ovarian cancer,

Methods

- Group 1 (n=170) – BENEFIT – Patient cohort defined as having received at least one treatment associated with potential benefit and no agents with potential lack of benefit.
- Group 2 (n=178) – LACK OF BENEFIT – Patient cohort defined as having received at least one agent with potential lack of benefit, while the "Lack of Benefit" cohort received at least one agent with death/censoring using the Kaplan-Meier method.

Results

- Of the remaining 348 eligible and evaluable patients, 303 were diagnosed with epithelial ovarian carcinoma, 26 with primary peritoneal carcinomas and 19 patients with fallopian tube carcinomas.
- The distribution of primary site of disease was similar between the two cohorts.
- There was significant difference in the distribution of histology between the two cohorts. Patients in the Benefit cohort experienced significantly longer post-profiling survival in ovarian cancer, compared with patients in the Lack of Benefit cohort (HR 0.54, 95% CI 0.37-0.80; p = 0.0018). Additionally, there was a trend toward longer overall survival in the Benefit cohort.

Conclusions

- We sought to determine whether tumor molecular profile-directed treatment in ovarian, primary peritoneal and fallopian tube cancer patients referred to Caris Life Sciences® between 2009 and March 2014 was performed. This subgroup analysis excluded 60 patients from the Analysis Population of 348, reducing the Benefit cohort to 140 and the Lack of Benefit cohort to 168. The median overall survival from the time of profiling performed for patients included in the Benefit cohort has not yet been reached but was significantly longer than patients included in the Lack of Benefit cohort who lived for a median of 32.6 months after profiling (HR 0.54, 95% CI 0.37-0.80; p<0.001).

Analysis population

- Total (n=348)
- Benefit cohort (n=170)
- Lack of Benefit cohort (n=178)

Anti-HER2 targeted therapies: trastuzumab, pertuzumab.

First-line chemotherapy: platinum [cisplatin or carboplatin] + taxane [docetaxel or paclitaxel] combination.

 second-line chemotherapy: vinorelbine, irinotecan, oxaliplatin.

Other therapies: bevacizumab, avastin, imatinib, sunitinib, sorafenib, vemurafenib, trametinib, cetuximab, combined mitoxantrone and prednisolone, gemcitabine, doxorubicin/liposomal-doxorubicin, tamoxifen.

Benefits of some profiling-directed agents by cohort

The table below shows select treatments associated with benefit with each lack of benefit according to the results of the DNA’s reports. More of the patients included in the Benefit cohort were predicted to have platinum and taxane resistance and may have received these treatments in an unplanned manner in line with standard care guidelines.

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- Median overall survival observed for patients included in the benefit cohort (158.0 months) compared to patients included in the Lack of Benefit cohort (43.4 months) treated towards significance (HR 0.54, 95% CI 0.37-0.80; p<0.001).

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References