Distinct molecular profiles and potential therapeutic targets in androgen receptor stratified ovarian cancer patients

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Abstract

Objectives: Growing literature in breast cancer suggests that androgen receptor (AR) expression can stratify patients with triple negative breast cancer (TNBC). Compared with AR+ TNBC, “quadruple negative” patients differ in their prognosis, response to therapy, and molecular profiles. It is unknown if AR status confers similar prognostic and treatment benefit in other tumor types. We aim to explore molecular and genomic features of AR+ and AR− ovarian cancer.

Methods: 8321 epithelial ovarian tumors were evaluated by Caris Life Sciences from 2009 to 2016 by mutliparameter profiling, which included protein expression (IHC), NextGen sequencing (SEQ), and/or in-situ hybridization. AR expression higher than (1+, 10%) was defined as AR+. We compared AR+ cases to AR− ovarian tumors.

Results

Figure 1. Overview of androgen receptor expression in 8321 epithelial ovarian tumors. Overall, positive AR expression was seen in 39% of EOC tumors (2338 of 8321); 35% in serous, 32% in endometrioid, 21% in carcinosarcoma, 4.3% in mucinous and 3.9% in clear cell histologies.

Figure 2. Comparison of prevalence of gene mutations (2A) and protein expression/ gene amplifications (2B) in ovarian tumors that are AR positive and negative. A star indicates statistical significance using Chi-square test.

Figure 3. Comparison of prevalence of gene mutations (3A) and protein expression/ gene amplifications (3B) in ER+/PR− ovarian tumors that are AR positive and negative. A star indicates statistical significance using Chi-square test.

Background

Growing literature in breast cancer suggests that androgen receptor (AR) should be used to stratify patients with triple negative breast cancer (TNBC). Compared with AR+ TNBC, “quadruple negative” patients differ in their prognosis, response to therapy, and molecular profiles. It is unknown if AR status confers similar prognostic and treatment benefit in other tumor types. We aim to explore molecular and genomic features of AR+ and AR− ovarian cancer.

Table: Summary tables for mutation (upper) and IHC/ISH (lower) seen in AR+ and AR− groups for the complete cohort and the ER+/PR− cohort

Conclusions

• Our findings suggest distinct molecular profiles in AR stratified ovarian cancer, providing potential targets for therapeutic exploitation.
• Drugs targeting the PI3K/Akt/mTOR, MAPK, CMET, and cell cycle control pathways, as well as hormonal agents, may benefit selected subsets of patients stratified by AR expression.

References

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