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Review Article

Targeting the hallmarks of ovarian cancer: The big picture

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HIGHLIGHTS

- Genomic instability and angiogenesis appear as the cornerstone in molecularly-driven therapy in high-grade serous OC.
- Targeting sustained proliferative signaling seems the most promising approach for low-grade and clear cell OC.
- Evasion of immune destruction is the emerging target in high-grade serous OC.

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ABSTRACT

Objective. As a result of relevant achievements in the field of translational research, several active drugs and multiple biological targets are available in ovarian cancer (OC). In this complex scenario, there is an urgent need to effectively summarize the available data in order to update conclusions, and outline perspectives.

Methods. The results in terms of target identification and drug development have been summarized using the well-known hallmarks of cancer firstly described, and recently modified by Hanahan and Weinberg [1–2]. Published data from clinical trials have been retrieved from PubMed, Embase, CINAHL and Cochrane database. Ongoing clinical trials were searched using clinicaltrials.gov web platform, and identified using NCT number.

Results. Genomic instability and angiogenesis are the most actively investigated hallmarks in high-grade serous OC, and the inhibition of tumor immune evasion appears as the emerging strategy for molecularly-driven therapy. Targeting sustained proliferative signaling through MEK and mTOR inhibitors seems the most promising approach in clear cell, and low-grade serous OC.

Conclusions. This substantial amount of data suggests that targeted therapies are already part of the clinical and therapeutic management of OC patients. The expectations of getting from translational research a better knowledge of tumor biology and therefore personalized drugs are high and worthy of maximum effort from referral centers.

Contents

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1. Introduction

In the last decade, the close and synergistic exchange between basic and clinical science has represented the cornerstone of research effort on ovarian cancer (OC). As a result of this global commitment, a plethora of active pharmaceutical compounds targeting different biological pathways have been actively tested in clinical trial on OC patients. In this big picture, there is an urgent need to effectively summarize the available data in ways that enable to update conclusions, and outline perspectives.

A conceptual approach to rationalize the complexity of cancer has been successfully introduced since 2000 by Hanahan and Weinberg

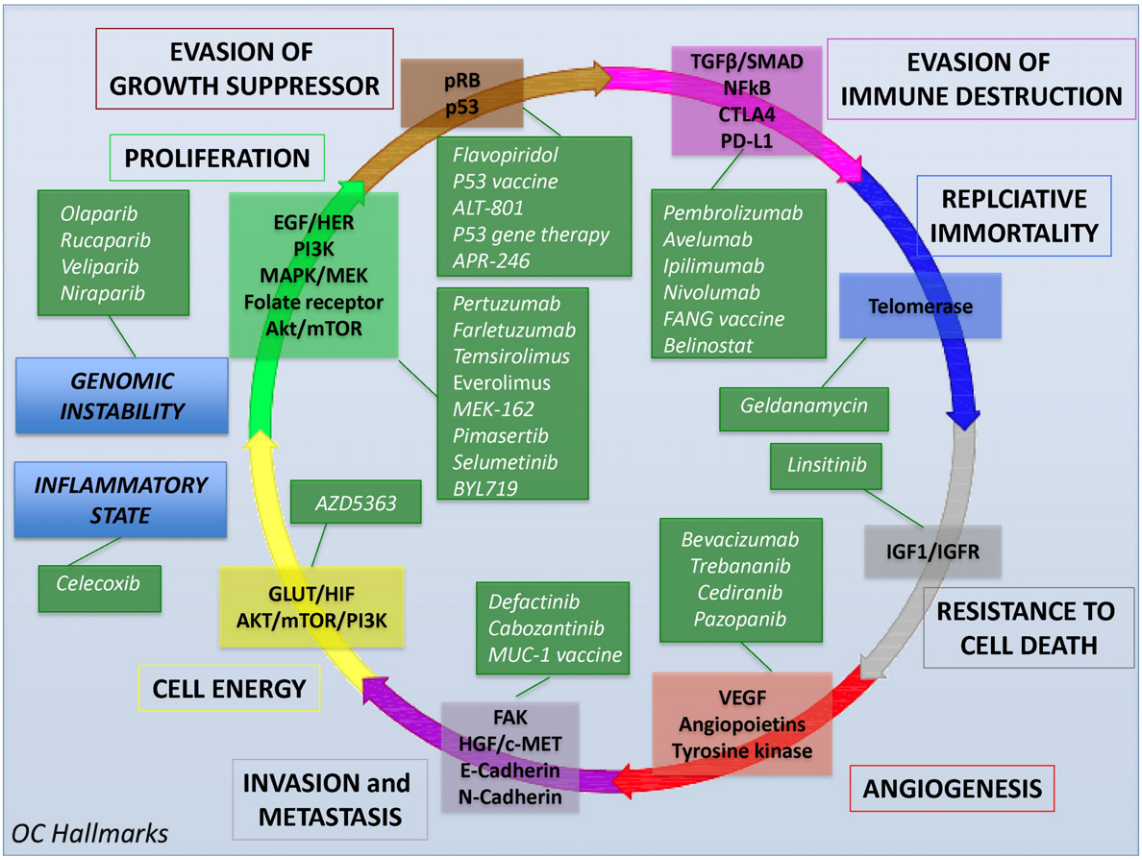

Fig. 1. Tumor hallmark and molecularly-driven drugs approved, or under evaluation in OC.