

76. Adrenal Cortical Carcinoma

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Emerging Prognostic Factors for Clinical Care

Targeted genetic analyses, such as sequencing and single-strand confirmation analyses, have identified somatic genetic changes in *TP53* located on 17p13. *TP53* is the most commonly mutated gene in ACC, and mutation is present in at least one third of ACCs. High-grade ACCs are enriched for mutations of *TP53* and/or *CTNNB1*, and these mutations tend to be mutually exclusive.

Risk Assessment Models

The AJCC recently established guidelines that will be used to evaluate published statistical prediction models for the purpose of granting endorsement for clinical use. Although this is a monumental step toward the goal of precision medicine, this work was published only very recently. For this reason, the existing models that have been published or may be in clinical use have not yet been evaluated for this cancer site by the Precision Medicine Core of the AJCC. In the future, the statistical prediction models for this cancer site will be evaluated, and those that meet all AJCC criteria will be endorsed.

Recommendations for Clinical Trial Stratification

Clinical trials for ACC should have the following:

- End point classification
- Intervention model
- Open label
- Primary purpose
- Documentation of:
 - Adverse events
 - Change in plasma cortisol levels
 - Change in objective measurement of tumor size
 - CT or MR imaging scans with RECIST (Response Evaluation Criteria In Solid Tumors)
 - Previous use of mitotane and mitotane levels
- Consideration of unstable medical condition.

Several current trials also are assessing ATR101, a selective small molecule inhibitor of sterol *O*-acyltransferase 1 (SOAT1) receptor. Chemotherapeutic drugs used in combination include streptozotocin, etoposide, doxorubicin, and cisplatin. Two combinations have been studied in the treatment of advanced adrenal cancer: a combination of mitotane and streptozotocin and a regimen

76. Adrenal Cortical Carcinoma

called EDP/M (etoposide, doxorubicin and cisplatin and mitotane). A large international phase III clinical trial is currently under way to compare these two therapies. There may be some risks associated with research; any trial must have an oversight committee.

Bibliography