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ADRENAL GLAND

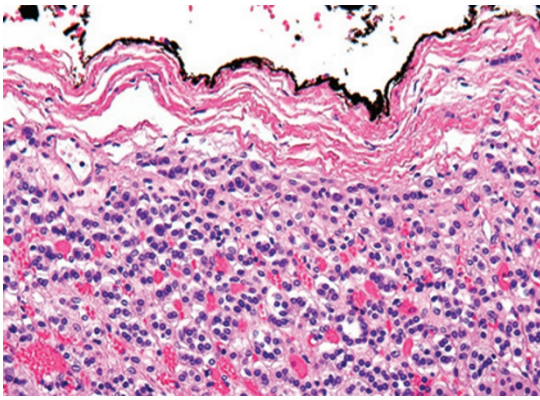
Adrenocortical carcinoma—first RCT

Results have been published for the FIRM-ACT trial of etoposide, doxorubicin, cisplatin and mitotane (EDP-M) versus streptozocin and mitotane in advanced adrenocortical carcinoma. "The main finding is clear," says Martin Fassnacht, the study's corresponding author. "EDP-M is superior to streptozocin plus mitotane and thus should be considered the standard first-line [cytotoxic] treatment in all patients with adrenocortical carcinoma."

The rarity of adrenocortical carcinoma (annual incidence rate 0.7–2.0 cases per million individuals) has greatly hampered previous research in this field. "Most participants in [the first international symposium on adrenocortical carcinoma, held in 2003] judged it unrealistic to organize an international trial with more than 300 patients," notes Fassnacht. "However, Britt Skogseid, Massimo Terzolo and myself accepted this challenge, and finally with the support of many, many investigators (mainly in Europe, but also in the USA, Canada and Australia) we finally succeeded." The study was eventually conducted in 12 countries and involved 304 adults from 40 tertiary centers. "We now have a very active study group," Fassnacht comments.

All outcomes were significantly better in the EDP-M group than in the streptozocin plus mitotane group: objective tumour response, 23.2% versus 9.2%; median progression-free survival 5.0 months versus 2.1 months; and 1-year survival 26.1% versus 7.2%. Rates of adverse events associated with the two therapies were similar. However, disease progression occurred in 92.1% of FIRM-ACT participants, and the improved antitumour efficacy of EDP-M did not translate into prolonged overall survival (14.8 months versus 12.0 months; $P = 0.07$). "Up to now, our knowledge about responses and progression-free and overall survival in adrenocortical carcinoma was scarce," remarks Fassnacht. "The FIRM-ACT study now provides the first robust data on these topics."

"Since there were no data on second-line treatments for adrenocortical carcinoma, we decided to integrate two phase II trials into our study," Fassnacht continues. "We offered all patients whose cancer progressed during first-line treatment the alternative treatment as second-line therapy." The performance of each regimen as second-line treatment was similar to that observed when it was given as first-line therapy.



"EDP-M is now the benchmark for all other new treatment options that hopefully will be developed," comments Fassnacht. "However, better therapies for this deadly disease are urgently needed."

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