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EDITORIAL

Eighth International Adrenal Cancer Symposium Brescia, Italy, September 30 to October 1–2, 2021

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Adrenocortical carcinoma (ACC) is an extremely rare malignancy, whose molecular pathogenesis is incompletely understood [1] and treatment strategies are limited [2]. An international Symposium, held in Ann Arbor in 2003 [3], stimulated international collaborations. Since then, the ACC international research community has grown over time and meets every 2 years in a Symposium where advances in the pathogenesis and therapy of this rare disease are discussed. The 8th edition of this Symposium was organized by Alfredo Berruti and Massimo Terzolo and was held in Brescia from September 30 to October 2, in a Webinar mode due to SARS COV-2 pandemic.

The webinar organization favored the widespread of Conference, which attracted more than 600 scientists from different countries. The 2021 meeting covered a broad range of topics related to advances in preclinical and clinical researches. It was organized in a number of sessions, aligned to a specific theme, research area or clinical issue. Sessions included lectures and oral communications on leading research related to molecular heterogeneity of adrenocortical tumors, new insights from preclinical studies, progress in surgical treatment, adjuvant therapies, management of advanced disease and future perspectives and proposals of new clinical studies. As previous editions, this productive Symposium served to educate, enhance discovery, and facilitate the development of effective strategies for this rare disease.

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This special issue of Endocrine contains five peer reviewed mini reviews which highlighted key topics discussed at the Conference.

Perge et al. [4] reviewed the available findings of liquid biopsy for assessing tumor heterogeneity in adrenocortical cancer. The authors pointed out that the investigation of markers of tumor heterogeneity in adrenocortical cancer is in the preliminary phase, but the few available studies provided some encouraging results. Circulating tumor cells and some circulating microRNAs appear to be the most promising modalities, but further studies on larger cohorts with uniform methodologies will be needed to assess the applicability of these techniques in the clinical setting.

Tamburello et al. [5] reviewed and discussed the available data on the potential role of FGF/FGFR signaling in adrenocortical development and tumorigenesis and its potential therapeutic impact in adrenocortical carcinoma. They underlined that FGF-1 and FGF-2 are expressed in the adrenal cortex and are the most powerful mitogens for adrenocortical cells. Physiologically, they are involved in development and maintenance of the adrenal gland and bind to a family of four tyrosine kinase receptors, among which FGFR1 and FGFR4 are the most strongly expressed in the adrenal cortex. The repeatedly proven overexpression of these two FGFRs also in adrenocortical cancer is likely a sign of their participation in proliferation and vascularization. The authors concluded that FGFRs potentially offer novel therapeutic targets also for adrenocortical carcinoma, a type of cancer resistant to conventional antimitotic agents.

The mini-review by Sigala et al. [6] provided information regarding newly established ACC cell lines. These authors correctly pointed out that until 2016 only 1 commercial cell line was available for clinical research: the NCI H295. From 2016 onwards there was a tremendous progress in this field with overall five new human adrenocortical cell lines developed: MUC-1, CU-ACC1, CU-ACC2, JIL-2266 and TVBF-7. This represents an important step forward in preclinical research as these cell lines differ from each other in having different molecular drivers that stimulate their growth and aggression.

The availability of these cell lines, therefore, makes it possible to design and perform experiments in a scenario of tumoral heterogeneity closer to what happens in the clinics.

In the paper entitled: "new endpoints in Adreno Cortical Carcinoma studies" Faron et al. [7] reviewed the potential surrogate endpoints that could potentially replace the true end point: overall survival (OS) in designing clinical trials and in clinical practice. Progression free survival (PFS) is currently the most used surrogate endpoints in ACC, although not validated yet. The radiologically assessed response according to RECIST criteria is a useful measure of treatment activity but there is uncertainty regarding its use as a surrogate efficacy parameter [8]. New endpoints are needed to better take into account the challenges offered by different clinical situations and treatment strategies. The authors highlighted the importance of patient-related endpoints, such as quality of life and patient reported outcomes [9], that are complementary to the efficacy measures: PFS and OS. These patient-related endpoints should be more considered in the near future.

Finally, the paper by Turla et al. [10], described the main side effects of the EDP-M scheme and the best way to manage them based on the experience of the Medical Oncology Unit of the Spedali Civili of Brescia [11]. The authors also also described strategies of safely administering of EDP-M in specific frail patients, such as those with huge disease extent and poor performance status (PS) and those with mild renal insufficiency. They concluded that a careful and accurate supportive care is essential to mitigate EDP-M side effects as much as possible and avoid that, due to toxicity, patients have to reduce doses and or postpone cytotoxic treatment with a negative impact on efficacy of this chemotherapy regimen.

In conclusion, the Brescia symposium provided the wider community with the opportunity to gain interesting insights into this rare disease and its current state-of-the-art research. We encourage interested researchers to join our community in order to increase research efforts and identify new effective treatments for ACC patients.

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