Adrenal cancer

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Milan, November 29 - December 1 2019
Conflict of interest

• None
Adrenocortical carcinoma (ACC)

<table>
<thead>
<tr>
<th>Tissue area</th>
<th>Hormones released</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zona glomerulosa (adrenal cortex)</td>
<td>Mineralocorticoids (regulate mineral balance)</td>
<td>Aldosterone</td>
</tr>
<tr>
<td>Zona fasciculata (adrenal cortex)</td>
<td>Glucocorticoids (regulate glucose metabolism)</td>
<td>Cortisol, Corticosterone, Cortisone</td>
</tr>
<tr>
<td>Zona reticularis (adrenal cortex)</td>
<td>Androgens (stimulate masculinization)</td>
<td>Dehydroepiandrosterone</td>
</tr>
<tr>
<td>Adrenal medulla</td>
<td>Stress hormones (stimulate sympathetic ANS)</td>
<td>Epinephrine, Norepinephrine</td>
</tr>
</tbody>
</table>

Pheochromocytoma & paraganglioma (PPGL)

Adrenal gland: 2 endocrinological neoplasms
Adrenocortical carcinoma at a glance

- Ultra-rare cancer, incidence 0.7 – 2 cases per 1,000,000 per year
- Bimodal age distribution:
  - First peak < 10 years
  - Second peak 4th-5th decade (mean age 45)
- ≈ 60% are metastatic at diagnosis
- 5-year survival rate: stage I-II 80% - stage III <50% - stage IV <15%
- >60% present hormonal hypersecretion
Hormone excess in ACC

- Cushing’s Syndrome: n=35 (56%)
- Virilization: n=13 (21%)
- Cushing’s + Virilization: n=6 (10%)
- Hyperaldosteronism: n=3 (5%)
- Feminization: n=5 (8%)

**Severe hypertension, hypokaliemia**

**Hirsutism, deepening of the voice, breast atrophy, male pattern baldness, clitoral hypertrophy, oligomenorrhea, altered libido**

**Gynecomastia, breast tenderness, decreased libido, testicular atrophy**

Cushing’s syndrome in ACC

• ACC + Cushing’s syndrome is a medical urgency

• Metabolic abnormalities:
  • Glucose intolerance/Diabetes
  • Osteoporosis/Fractures
  • Hypertension/cardiomypathy
  • Refractory hypokaliemia

• Immune deficiency (lymphocytotoxic effect of glucocorticoids)

• Psychiatric disorders

• First treat cortisol excess!
Diagnosis of ACC: ESMO/ENSAT proposed workup

**Hormonal work-up**
- Glucocorticoid excess (minimum 3 of 4 tests)
  - Dexamethasone suppression test (1 mg, 23:00 h)
- Excretion of free urinary cortisol (24 h urine)
  - Basal cortisol (serum)
  - Basal ACTH (plasma)
- Sexual steroids and steroid precursors
  - DHEA-S (serum)
  - 17-OH-progesterone (serum)
  - Androstenedione (serum)
  - Testosterone (serum)
- 17-beta-estradiol (serum, only in men and postmenopausal women)
- 24-h urine steroid metabolite examination

**Mineralocorticoid excess**
- Potassium (serum)
- Aldosterone/renin ratio (only in patients with arterial hypertension and/or hypokalemia)

**Catecholamine excess**
- Normetanephrine, metanephrine, and methoxytyramine (plasma)
- Alternatively: fractionated metanephrine excretion (24 h urine)

**Imaging**
- CT or MRI of abdomen and CT thorax
- Bone scintigraphy (when suspecting skeletal metastases)
- FDG-PET (optional)
  - MIBG scintigraphy, DOTA-TATE-PET, Dopa/Dopamine PET or FDG-PET if pheochromocytoma is proved

Surgery is the mainstay of therapy and represents the only chance of cure in ACC

ACC – ESE/ENSAT Practice Guidelines 2018

1.3. Surgery for suspected localized ACC

R.3.1. We recommend that adrenal surgery for suspected/confirmed ACC should be performed only by surgeons experienced in adrenal and oncological surgery.

R.3.2. We recommend complete en bloc resection of all adrenal tumors suspected to be ACC including the peritumoral/periadrenal retroperitoneal fat. We recommend against enucleation and partial adrenal resection for suspected ACC. If adjacent organs are suspected to be invaded, we recommend en bloc resection. However, we suggest against the routine resection of the ipsilateral kidney in the absence of direct renal invasion.

R.3.3. Open surgery is the standard surgical approach for confirmed or highly suspected ACC. Therefore, we recommend open surgery for all tumors with radiological findings suspicious of malignancy and evidence for local invasion.

**Stage stratification**

<table>
<thead>
<tr>
<th>ENSAT stage</th>
<th>TNM</th>
<th>Definition</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>T1, N0, M0</td>
<td>Tumor ≤5 cm</td>
<td>2%</td>
</tr>
<tr>
<td>II</td>
<td>T2, N0, M0</td>
<td>Tumor &gt;5 cm</td>
<td>19%</td>
</tr>
<tr>
<td>III</td>
<td>T1–T2, N1, M0</td>
<td>Lymph node involvement and/or tumor infiltration into surrounding tissue and/or a tumor thrombus in the vena cava and/or renal vein</td>
<td>18%</td>
</tr>
<tr>
<td>IV</td>
<td>T1–T4, N0–N1, M1</td>
<td>Metastatic disease</td>
<td>61%</td>
</tr>
</tbody>
</table>

Potentially curable (39%)
Which surgery?

- Two different approaches are possible for adrenalectomy:
  - Open surgery adrenalectomy (OA)
  - Laparoscopic adrenalectomy (LA)
- No prospective trials are available to determine which is the best strategy
Survival Analysis

Brix et al. EAU 2010
Peritoneal Dissemination
A Complication of Laparoscopic Surgery

Peritoneal dissemination
[266 patients referred to the NCI with recurrence of disease and with extensive follow-up information]

Peritoneal dissemination > Laparoscopy: 21/44 (47%)
Peritoneal dissemination > Open Resection: 7/222 (3.1%)

RR 15.1 [6.8-33.4] p <0.0001
Prognostic factors

1.5. Staging classification and prognostic factors

R.5.1. At initial diagnosis, we recommend using the European Network for the Study of Adrenal Tumours (ENSA) staging classification (+++O).

R.5.2. At initial diagnosis, we recommend taking the following factors into account when assessing the prognosis and treatment options: tumor stage, resection status, Ki67 index (or mitotic count), autonomous cortisol secretion and the patient’s general condition (++OO).

R.5.3. During follow-up, we recommend re-assessing prognosis at each evaluation, to guide treatment strategy (++OO).
Prognostic factors

Surgery\(^1\)

![Surgery Survival Graph]

ENSAT Stage\(^2\)

![ENSAT Stage Survival Graph]

Ki-67\(^3\)

Validation cohort

![Ki-67 Validation Graph]

Cortisol hypersecretion (Cushing’s s)\(^4\)

![Cortisol Hypersecretion Graph]


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Prognostic factors in ACC: GRAS score

G = grade (Weiss score <6 or >6 or Ki67 <20% or >20%)
R = resection status of the primary
A = age younger than or older than 50 years
S = hormone-related symptoms at diagnosis

GRAS favorable:  Ki67 <20%, primary R0 resection, age <50 y, no symptoms
GRAS unfavorable:  Age >50 y, or presence of symptoms
GRAS pejorative:  Ki67 >20% and/or primary R1-2 resection status
Recurrence rate in ACC is high

**RECURRENT RATE**

<table>
<thead>
<tr>
<th>Study</th>
<th>Recurrence Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crucitti et al., 1996</td>
<td>23%</td>
</tr>
<tr>
<td>Bellantone et al., 1997</td>
<td>37%*</td>
</tr>
<tr>
<td>Abiven et al., 2006</td>
<td>40%**</td>
</tr>
<tr>
<td>Gonzales et al., 2007</td>
<td>73%</td>
</tr>
<tr>
<td>Dy et al., 2013</td>
<td>74%</td>
</tr>
<tr>
<td>Ayala-Ramirez, Jasm et al., 2013</td>
<td>66%</td>
</tr>
<tr>
<td>Amini et al., 2016</td>
<td>64%</td>
</tr>
</tbody>
</table>

* Disease recurred in 52 (37%) of 140 patients who underwent radical surgery
** 2 years after diagnosis, 40% of stage I-III patients had developed distant metastasis
ESE/ENSAT algorithm in adjuvant therapy

**ACC amenable to complete resection**

- Complete resection (R0)
- Rx or R1 resection

**ENSAT I-II and Ki67 ≤10%**
- Low/intermediate risk
  - Consider mitotane

**ENSAT III-IV or Ki67 >10%**
- High risk
  - Adjuvant mitotane

**Follow-up every 3 months**: imaging and tumor markers

**Tumor free**
- DFI > 12 months + completely resectable

**Recurrence**
- DFI < 6 months or not resectable
  - See figure 4

Fassnacht et al. Eur J Endocrinol 2018
Toxicity of Mitotane

TABLE 4. Adverse effects during mitotane treatment

<table>
<thead>
<tr>
<th>Adverse effect</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastrointestinal: nausea, vomiting, diarrhea, anorexia, mucositis</td>
<td>Very common</td>
</tr>
<tr>
<td>CNS: lethargy, somnolence, vertigo, ataxia confusion, depression, dizziness, decreased memory, polyneuropathy</td>
<td>Very common, common</td>
</tr>
<tr>
<td>Adrenal insufficiency</td>
<td>Very common</td>
</tr>
<tr>
<td>Primary hypogonadism in men</td>
<td>Common</td>
</tr>
<tr>
<td>Gynecomastia</td>
<td>Common</td>
</tr>
<tr>
<td>Skin rash</td>
<td>Common</td>
</tr>
<tr>
<td>Autoimmune hepatitis</td>
<td>Rare</td>
</tr>
<tr>
<td>Cardiovascular: hypertension</td>
<td>Very rare</td>
</tr>
<tr>
<td>Ocular: blurred vision, double vision, toxic retinopathy, cataract, macular edema</td>
<td>Very rare</td>
</tr>
<tr>
<td>Hemorrhagic cystitis</td>
<td>Very rare</td>
</tr>
<tr>
<td>Increase of hepatic enzymes (in particular γ-GT)</td>
<td>Very common</td>
</tr>
<tr>
<td>Increase in hormone binding globulins (CBG, SHBG, TBG, vitamin D binding protein)</td>
<td>Very common</td>
</tr>
<tr>
<td>Disturbance of thyroid parameters (interference with binding of T₄ to TBG, total T₄ ↓)</td>
<td>Very common</td>
</tr>
<tr>
<td>Hypercholesterolemia, hypertriglyceridemia</td>
<td>Very common</td>
</tr>
<tr>
<td>Prolonged bleeding time</td>
<td></td>
</tr>
<tr>
<td>Leucopenia</td>
<td>Common</td>
</tr>
<tr>
<td>Thrombocytopenia, anemia</td>
<td>Rare</td>
</tr>
<tr>
<td>Hematuria, albuminuria</td>
<td>Very rare</td>
</tr>
<tr>
<td>Hepatic microsomal enzyme induction with increased metabolism of glucocorticoids and other steroids and barbiturates, phenytoin, warfarin</td>
<td>Very common, common</td>
</tr>
</tbody>
</table>

Allolio et al. J Clin Endocrinol Metab 2006
Adjuvant Mitotane for operated ACC: update 2017

Long-Term Outcomes of Adjuvant Mitotane Therapy in Patients With Radically Resected Adrenocortical Carcinoma

Alfredo Berruti, Salvatore Grisanti, Alina Pulzer, Melanie Claps, Fulvia Daffara, Paola Loli, Massimo Mannelli, Marco Boscaro, Emanuela Arvat, Guido Tiberio, Stefanie Hahner, Barbara Zaggia, Francesco Porpiglia, Marco Volante, Martin Fassnacht, and Massimo Terzolo

Berruti et al. J Clin Endocrinol Metab 2017
ESE/ENSAT algorithm in adjuvant therapy

**ACC amenable to complete resection**

- **Complete resection (R0)**
  - Low/intermediate risk: Consider mitotane
  - High risk: Adjuvant mitotane

- **Rx or R1 resection**
  - Adjuvant mitotane + consider radiation therapy

**ADIUVO I trial**

- Follow-up every 3 months: imaging and tumor markers
  - Tumor free
  - Recurrence
    - DFI > 12 months + completely resectable
    - DFI < 6 months or not resectable See figure 4

Fassnacht et al. Eur J Endocrinol 2018

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Mitotane is a “slow” drug

• The so called “therapeutic range” (14-20 μg/ml) is attained within 3 months
• Approximately 50% of patients never reach the therapeutic range

• Is adjuvant Mitotane adequate for an ACC with high proliferative activity (Ki67)?
European Society of Endocrinology/ENSAT algorithm in ACC

ACC amenable to complete resection\(^1\)

- Complete resection (R0)
- ENSAT I-II and Ki67 ≤10\(^%\)^\(^3\)
  - Low/intermediate risk
  - Consider mitotane\(^4\)
- ENSAT III-IV or Ki67 >10\(^%\)^\(^3\)
  - High risk
  - Adjuvant mitotane\(^5\)

- Rx or R1 resection\(^2\)
  - Adjuvant mitotane + consider radiation therapy

ADIUVO I trial

Surgery

Follow-up every 3 months\(^6\): imaging and tumor markers

- Tumor free
- Recurrence
  - DFI > 12 months + completely resectable
  - DFI < 6 months\(^7\) or not resectable
    - See figure 4

ADIUVO II trial

Fassnacht et al. Eur J Endocrinol 2018

Always consider clinical trials

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ADIUVO-2 trial (NCT: NCT03723941)

# Patients: 200

Stratification
- Ensat stage (I/II vs. III)
- Surgery
- Ki67 (10%-20% vs >20%)

Random

- Cisplatin + Etoposide
  ± Mitotane
- ± Mitotane

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What happens after surgery?

Surgery of adrenal or extra-adrenal mass

ACC
- Approx 70-80% M1 within 2 years

PPGL
- Malignant PPGL
  - Adrenal Pheo: 10%
  - Extra-adrenal Pheo: 35%
  - M1 within 1 year

Lung 45%
Liver 42%
Lymphnodes 24%
Bone 13%
Peritoneum, Locoregional 50%

Bone >60%
Lymphnodes 40%
Lung 30%
Liver 26%
R.8.4. In patients with advanced ACC at the time of diagnosis not qualifying for local treatment, we recommend either mitotane monotherapy or mitotane+EDP depending on prognostic parameters (+++O).

R.8.6. We recommend EDP-M as first-line treatment if the time interval between last surgery/loco-regional therapy and recurrence is less than 6 months (++00), rather than repeat loco-regional measures.

R.8.8. In patients who progress under mitotane monotherapy, we recommend to add EDP (+++O).
Backbone of treatment is mitotane or chemo + mitotane

- **Stage IV ACC**
  - **PS 2** (Low tumor burden, slowly progressing)
  - Mitotane monotherapy + local regional options + chemotherapy (1 drug or 2 drugs)
  - EDP-M for non secreting ACC
  - EDP-M-Methyrapone for secreting ACC
  - **PS 0-1** (High tumor burden, rapidly progressing)
  - EDP-M
The EDP-M schedule

- This scheme incorporated all of the drugs active in ACC in 1990

Berruti et al. Tumori 1992
The FIRM-ACT trial: results

Fassnacht et al. NEJM 366(23):2189-97; 2012

EDP-M median PFS: 5.0 months
Sz-M median PFS: 2.1 months

EDP-M median OS: 14.8 months
Sz-M median OS: 12.0 months

Hazard ratio, 0.55 (95% CI, 0.42–0.68)
P<0.001 by log-rank test

Hazard ratio, 0.79 (95% CI, 0.61–1.02)
P=0.07 by log-rank test
EDP-M: Brescia experience
What is the advantage of combining mitotane and chemo?

Chemotherapy can obtain a disease control in the early months

3 months are needed for the levels of mitotanemia to reach therapeutic concentrations
We Should Desist Using RECIST, at Least in GIST
Robert S. Benjamin, Haesun Choi, Homer A. Macapinlac, Michael A. Burgess, Shreyaskumar R. Patel, Lei L. Chen, Donald A. Podoloff, and Chuttip Charnsangavej

Time to progression curves

**A**

**B**

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What is the best way to assess tumor response?
RECIST vs CHOI

Multimodality tumor tracking software (Philips Intellispace Portal v8.0)

PR RECIST
PR CHOI

PD RECIST
PR CHOI
CHOI vs RECIST and overall survival in ACC

29 patients

Overall Survival according to RECIST criteria

Overall Survival according to CHOI criteria

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ESE/ENSAT guidelines on advanced ACC

Advanced ACC not amenable to radical resection

- Always consider clinical trials
- Debulking surgery

No prior systemic therapy

Recurrence during adjuvant mitotane

Mitotane +/- local therapies

Mitotane + EDP

Local therapies + mitotane

Follow-up every 2-3 months

Partial response or stable disease: continue therapy + consider surgery

Progressive disease

Mitotane plus EDP or local therapies

Consider additional therapy

Mitotane plus EDP
Prognostic role of debulking surgery after disease response to EDP-M in advanced ACC

**Progression Free Survival**
- Not Surgery: Median 6.87 m. (0.07-23.20)
- Surgery: Median 13.77 m. (1.83-21.37)

Log-rank p < .005

**Overall Survival**
- Not Surgery: Median 10.83 m. (0.57-69.37)
- Surgery: Median 42.16 m. (6.6-42.17)

Log-rank p < .0005
How can we best use EDP?

• If possible, do not reduce the doses (Medical Oncology hands, G-CSF, hormonal supportive therapies, …)

• Disease progression after 2-3 months does not necessarily mean a failure

• Consider debulking surgery, if residual disease after EDP is $\leq 10\%$
Overall poor response rate to chemo & target therapy in ACC

<table>
<thead>
<tr>
<th>Study</th>
<th>Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Henning, 2017</td>
<td>Gemcitabine and capecitabine</td>
</tr>
<tr>
<td>Fassnacht, 2012 A</td>
<td>Etoposide, doxorubicin, cisplatin, and mitotane</td>
</tr>
<tr>
<td>Fassnacht, 2012 B</td>
<td>Streptozocin and mitotane</td>
</tr>
<tr>
<td>Hermsen, 2011</td>
<td>Mitotane and different cytotoxic drug</td>
</tr>
<tr>
<td>Fassnacht, 2015</td>
<td>Linsitinib</td>
</tr>
<tr>
<td>Berruti, 2005</td>
<td>Etoposide, doxorubicin, cisplatin, and mitotane</td>
</tr>
<tr>
<td>Gonzalez, 2007</td>
<td>Mitotane</td>
</tr>
<tr>
<td>Williamson, 2000</td>
<td>Cisplatin and etoposide</td>
</tr>
<tr>
<td>Bukowski, 1993</td>
<td>Cisplatin and mitotane</td>
</tr>
<tr>
<td>Decker, 1991 B</td>
<td>Mitotane</td>
</tr>
<tr>
<td>Abraham, 2002</td>
<td>Doxorubicin, etoposide, vincristine, and mitotane</td>
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<tr>
<td>Sperone, 2010</td>
<td>Gemcitabine and capecitabine/5-fluorouracil</td>
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<td>Kroiss, 2012</td>
<td>Sunitinib</td>
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<tr>
<td>Naing, 2013</td>
<td>Cixutumumab and temsirolimus</td>
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<td>Haak, 1994</td>
<td>Mitotane</td>
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<tr>
<td>Kroiss, 2016</td>
<td>Trofosfamide</td>
</tr>
<tr>
<td>Bonacci, 1998</td>
<td>Etoposide and cisplatin</td>
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<td>Urup, 2013</td>
<td>Cisplatin and docetaxel</td>
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<tr>
<td>Decker, 1991 A</td>
<td>Doxorubicin</td>
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<td>Lerario, 2014</td>
<td>Cixutumumab and mitotane</td>
</tr>
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<td>Haluska, 2010</td>
<td>Figitumumab</td>
</tr>
<tr>
<td>Schlumberger, 1991</td>
<td>5-fluorouracil, doxorubicin, and cisplatin</td>
</tr>
<tr>
<td>O’Sullivan, 2014</td>
<td>Axitinib</td>
</tr>
<tr>
<td>Baudin, 2001</td>
<td>Mitotane</td>
</tr>
<tr>
<td>Baudin, 2002</td>
<td>Irinotecan</td>
</tr>
<tr>
<td>Kahn, 2004</td>
<td>Vincristine, teniposide, cisplatin, and cyclophosphamide</td>
</tr>
<tr>
<td>Wortmann, 2010</td>
<td>Bevacizumab and capecitabine</td>
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<tr>
<td>Quinkert, 2008</td>
<td>Erlotinib</td>
</tr>
<tr>
<td>Berruti, 2012</td>
<td>Sorafenib and metronomic paclitaxel</td>
</tr>
</tbody>
</table>

Fassnacht et al. Eur J Endocrinol 2018
MSI-H & DNA repair genes in ACC

Analysis of Microsatellite Instability

TCGA analysis of DNA damage repair genes mutations

1Bonneville et al. JCO Precis Oncol 2018; 2Ding et al. Cell 2018;

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# Immunotherapy vs CT trials in advanced ACC

<table>
<thead>
<tr>
<th>Author/year</th>
<th>N. pts</th>
<th>N. previous lines</th>
<th>ICI agent</th>
<th>CR (%)</th>
<th>PR (%)</th>
<th>SD (%)</th>
<th>CBR (%)</th>
<th>6-PFS</th>
<th>Median OS</th>
<th>Response criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Raj/2019</td>
<td>39</td>
<td>1</td>
<td>Pembrolizumab</td>
<td>0 (0)</td>
<td>9 (23)</td>
<td>7 (18)</td>
<td>16 (41)</td>
<td>20%</td>
<td>25 mo</td>
<td>RECIST</td>
</tr>
<tr>
<td>Habra/2019</td>
<td>14</td>
<td>≥2</td>
<td>Pembrolizumab</td>
<td>0 (0)</td>
<td>2 (14)</td>
<td>7 (50)</td>
<td>9 (64)</td>
<td>36%</td>
<td>NR</td>
<td>IR-RECIST</td>
</tr>
<tr>
<td>Le Tourneau/2018</td>
<td>50</td>
<td>≥2</td>
<td>Avelumab</td>
<td>0 (0)</td>
<td>3 (6)</td>
<td>21 (42)</td>
<td>24 (48)</td>
<td>21%</td>
<td>10.6 mo</td>
<td>RECIST + IR-RECIST</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>103</strong></td>
<td></td>
<td></td>
<td>0 (0)</td>
<td><strong>14 (13)</strong></td>
<td><strong>35 (34)</strong></td>
<td><strong>49 (47)</strong></td>
<td><strong>25.6%</strong></td>
<td><strong>18 mo</strong></td>
<td></td>
</tr>
</tbody>
</table>

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<thead>
<tr>
<th>Author/year</th>
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<th>6-PFS</th>
<th>Median OS</th>
<th>Response criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sperone/2010</td>
<td>28</td>
<td>≥2</td>
<td>Gemcitabine/Capecitabine</td>
<td>0 (0)</td>
<td>1 (4.9)</td>
<td>11 (39)</td>
<td>13 (46)</td>
<td>50%</td>
<td>10 mo</td>
<td>RECIST</td>
</tr>
<tr>
<td>Henning/2017</td>
<td>132</td>
<td>≥2</td>
<td>Gemcitabine/Capecitabine</td>
<td>0 (0)</td>
<td>7 (5.3)</td>
<td>36 (27)</td>
<td>43 (32)</td>
<td>30%</td>
<td>NR</td>
<td>RECIST</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>160</strong></td>
<td></td>
<td></td>
<td>0 (0)</td>
<td>8 (5)</td>
<td><strong>47 (29)</strong></td>
<td><strong>56 (35)</strong></td>
<td><strong>40%</strong></td>
<td><strong>10 mo</strong></td>
<td></td>
</tr>
</tbody>
</table>

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**Flyer Rare Tumours (30 Aug)_screen 30.08.2016 13:19 Pagina 3**
Drivers of immunotherapy resistance in ACC

Cosentini et al. Endocrin Conn 2018
Multiplatform genomic insights from TCGA/ENSAT offer a rational way to patient stratification & target therapy

Mohan et al. Curr Opin Endocrin Metab Res. 2019

Milan, November 29 - December 1 2019
European Society of Endocrinology Clinical Practice Guidelines on the management of adrenocortical carcinoma in adults, in collaboration with the European Network for the Study of Adrenal Tumors

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