NeuroEndocrine Tumors
Diagnostic and therapeutic challenges: Pancreatic NET
Case presentation @ ESMO preceptorship - Singapore

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Real story – all facts are correct and real
AR - man born in 1941
Medical history

• 02/2001:
  – diagnosis well differentiated NET of the pancreas body and tail with hypercalcemia – no evidence of metastases
  – PTH low
  – Inoperable during laparotomy because of vessel invasion (city X)
  – R/ octreotide & pamidronaat
  – Later: alfa interferon

• 2004:
  – referral to Leuven: because of local disease progression
  – Laparotomy: extensive resection (pancreas, surrenal gland, spleen & lymphnodes)
  – Histology: well differentiated NET; Ki67:15%; negative LN and negative resection margins (2 mm)
  – No adjuvant treatment
  – Postoperative normalisation of hypercalcemia
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Medical history

• 2007 :
  – Hypercalcemia till 14.1 mg/dl – Vit D nl; PTH very low
  – Decreased renal function
  – Locoregional relapse with multiple liver metastases and abdominal lymph nodes
  – Octreoscan: positive
  – R/ start octreotide LAR 20mg q4w; later increase to 30 mg q4w
  – Hypercalcemia manageable

• 2008 :
  – Tumor progression and further increase of serum calcium
  – Atrioventricular block: 2nd degree
  – stop octreotide
  1/2008 to 06/2009 : 3x intrahepatic chemoembolisations (city X)
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Medical history

- 2009 : Leuven
  - Hypercalcemia frequent episodes till >14 mg/dl
  - 25-OH-vitamin D : 20.2 µg/L (7.0 - 60.0)
  - 1,85 PTH very low : < 0.1 ng/L (3.0 - 40.0)
  - Hypercalcemia and hypofosfatemie in framework of HHM (humoral hypercalcemia of malignancy) caused by production of PTH-related peptide.
  - Treated with intermittently diuretics; rehydratation; low dose biphosphonates; a few times calcitonin and corticosteroids
  - Decreased renal function

- Imaging: progression locoregional relapse with multiple levermetastases and abdominal lymphnodes
- Octreoscan: positive
- Exclusion for PRRT (Yttrium in Leuven)
AR - MAN BORN IN 1941
discussion
AR - man born in 1941
Medical history

- **July 2009:**
  - Start sunitinib 37.5 mg/day
  - Good tolerance
  - Fast normalisation of hypercalcemia
  - Clear regression on imaging

- **12/2009:**
  - Nefrotic syndrome with proteinuria -14 g/d - and increase in serum creatinine
  - Kidney biopsy → focal sclerosis
    - compatible with secondary changes to sunitinib
  - **Sunitinib stopped.**
  - Proteinuria improved till 2-3 g/d
Serum Calcium - 11/2007 - 12/2009

mg/dl

Nefrotic syndrome

SUNITINIB

Calcium
Creatinine
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Medical history

• 02/2010 - 04/2010
  – acute coronary syndrome and ischemic cardiac decompensation, EF 50%

• 05/2010:
  – Relapse hypercalcemia
  – Proteinuria persistent: 2-3 g/d
  R/intermittent including: rehydration diuretics, corticosteroids, calcitonin, pamidronate
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Medical history

- 30/08/2010:
  - Imaging: progressive disease and persistent, refractory hypercalcemia
  - R/ Restart sunitinib 25 mg/d after extensive discussion and also at request of patient and family
  - Fast normalisation of hypercalcemia

- 17/09/2010:
  - Acute deterioration of renal function
  - NSTEMI → stop sunitinib
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Medical history

• 30/08/2010:
  – Imaging: progressive disease and persistent, refractory hypercalcemia
    R/ **Restart sunitinib** 25 mg/d after extensive discussion and also at request of patient and family

• 17/09/2010:
  – acute renal failure, NSTEMI → **stop sunitinib**

• Coronarography:
  – Right coronary art.: slightly narrowed.
  – Main coronary art.: no relevant abnormalities
  – Left anterior descendens, circumflex & ramus intermedius: severe stenoses
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Medical history

- **17/09/2010:**
  - acute renal failure, NSTEMI → stop sunitinib
  - Proteinuria persistent

- **October/November 2010:**
  - Relapse Refractory Hypercalcemia
  - Serum creatinine increase
  - AngioMRI (total body): slight increase of tumor load
**Serum calcium 08/2010 - 11/2010**

- **Calcium**
- **Creatinine**

- **Sunitinib (epidose 2)**

![Graph showing serum calcium levels from 08/2010 to 11/2010 with a peak around 11/2010. The graph indicates a significant increase in calcium levels after the start of Sunitinib treatment.](image-url)
discussion
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Medical history

• 17/09/2010:
  – acute renal failure, NSTEMI → stop sunitinib
  – Serum creatinine
  – Proteinuria persistent

• October/November 2010:
  – Relapse Refractory Hypercalcemia
  – Serum creatinine increase
  – AngioMRI (total body): slight increase of tumor load

• End November 2010:
  – Start everolimus 10 mg/day
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Medical history

• End november 2010:
  – Start everolimus 10 mg/day

• January 2011:
  – Calcium normalized
  – Acute nose bleeding+++ with decrease in Hemoglobin till 6.2 g/dl, with secondary NSTEMI
    probably secondary to mucositis++ (everolimus related?)
  – Stop everolimus early january
Serum Calcium 11/2010 – 03/2011

Everolimus 10 mg

- 5/12/2010
- 9/12/2010
- 16/12/2010
- 30/1/2011
- 13/2/2011
- 20/2/2011
- 27/2/2011

Calcium

Creatinine
discussion
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  – Start everolimus 10 mg/day

• January 2011:
  – Calcium normalized
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  – probably secondary to mucositis++ (everolimus related?)
  – Stop everolimus early january

• March 3, 2011
  – Hypercalcemia: 12.5 & 13.1 mg/dl
  – Restart everolimus at a dose of 5 mg/day
Serum Calcium 11/2010 – 03/2011

- Everolimus 10 mg
- Everolimus 5 mg

mg/dl
Mr AR and his family are extremely grateful for progress in treatment options for PNET.