



Clinical Cases Discussion

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Cancer Center

- Speaker: Bayer, Janssen, Astellas, BMS, Merck, MSD, Astra Zeneca, Pfizer
- Sub investigator in sponsored clinical trials: Boehringer Ingelheim, MSD, Janssen, BMS
- Principal investigator in sponsored clinical trials : BMS, Astra Zeneca
- Advisory Board: BMS, Janssen



- MN, 83 years old, Asian, ECOG=1
- Comorbidities: Hypertension, Coronary Arterial Disease (previous revascularization and coronary stents) both controlled and asymptomatic
- 2000: Diagnosis of Prostate Cancer
- cT2aN0M0, Gleason 4+3, Initial PSA=281
- Radiotherapy + 3 years androgen deprivation therapy (goserelin) → nadir PSA=0,6
- Biochemical Recurrence: Intermittent ADT



- 06/2013: Biochemical Progression (PSA=4,13) + bone metastasis
Bicalutamide + goserelin + zoledronic acid
- 08/2013: Biochemical (PSA=24) and radiological progression (bone)
Abiraterone + Prednisone
- 02/2014: Biochemical (PSA=43) + Radiological Progression (bone)
Docetaxel x 5 cycles → Unacceptable Toxicity (PSA=53)

- 09/2014: Biochemical (PSA=91) + Clinical Progression
Oral Cyclophosphamide + dexamethasone – no response
- 01/2015: Biochemical (PSA=380) + Radiological Progression (bone)
Cabazitaxel x 10 cycles up to 08/2015 (PSA=77)
- 11/2015: Biochemical (PSA=96) + Clinical Progression
Enzalutamide with PSA Response (PSA=4,89)



- 01/2017: Biochemical (PSA=22) + Radiological Progression (bone) + Clinical Progression
- Laboratory Results:
PSA=22 Testosterone<0,03 ALP=247 LDH=386 (ULN 225)
CEA=2,0
Hb=13,6 Leucocytes=4450 Platelets=145000
No renal or hepatic dysfunctions
- Pain medications: Oral Morphine 15 mg / day

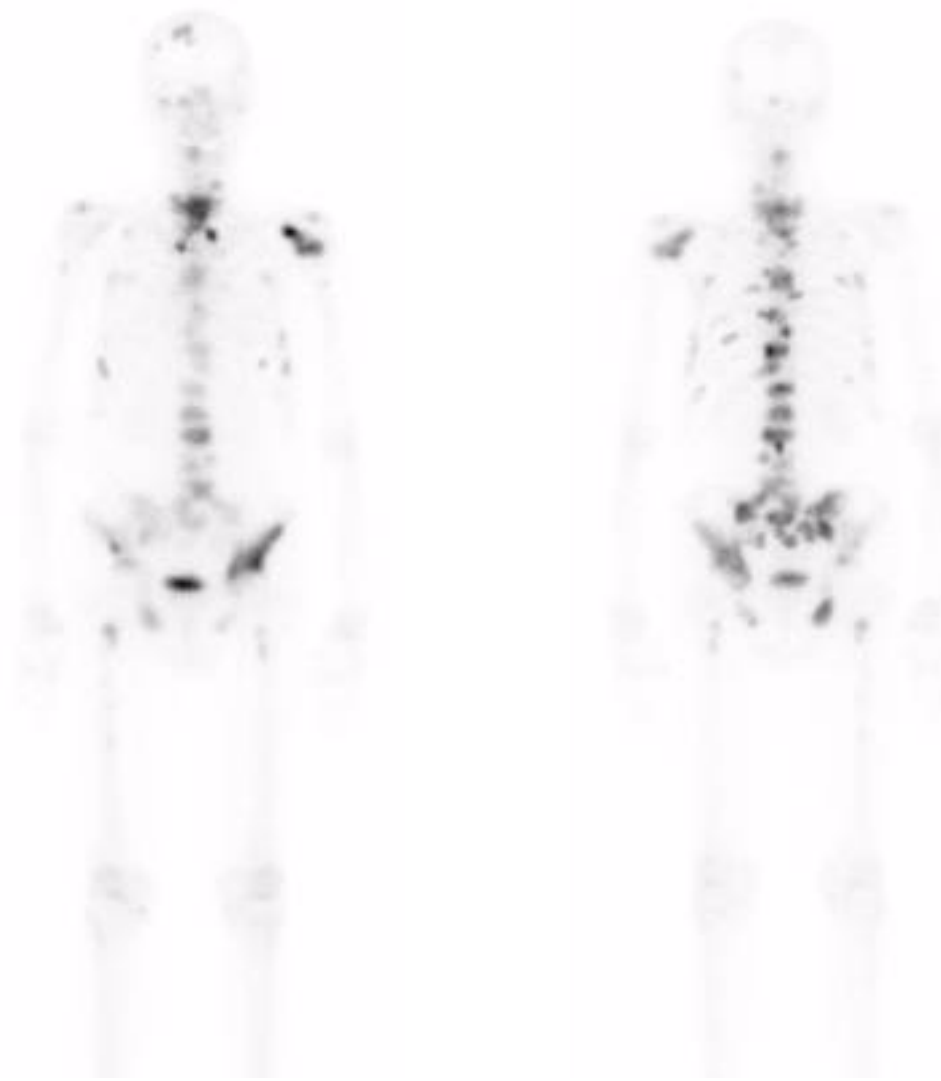


Clinical Case 1 – Bone Scan



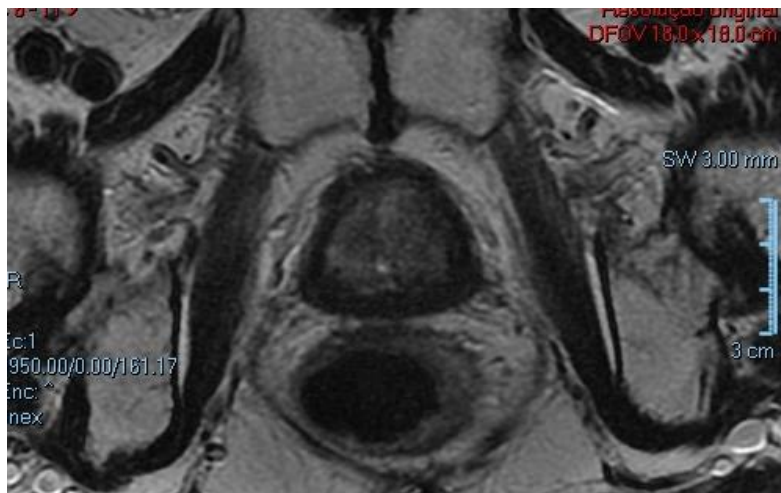


Clinical Case 1 – Bone Scan



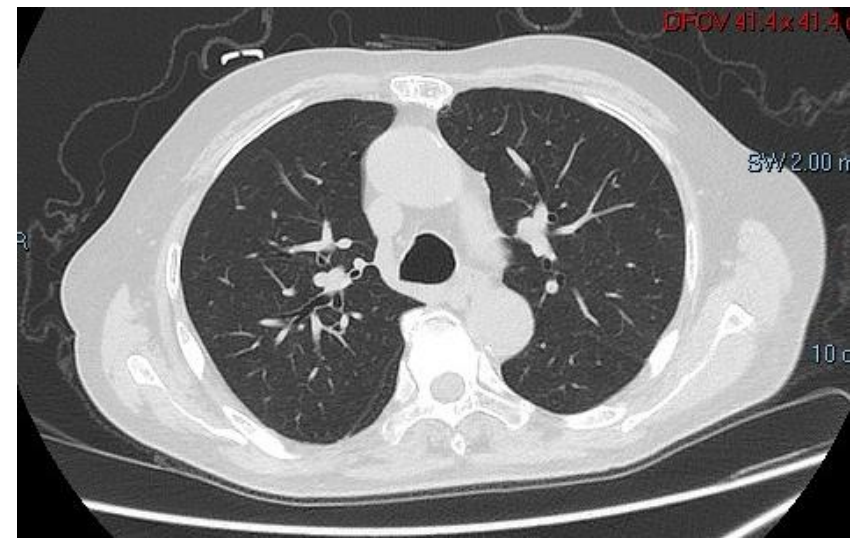


Clinical Case 1 – MRI A/P





Clinical Case 1 – Thorax CT



- Symptomatic castration resistant prostate cancer metastatic to the bones, ECOG=1
- Previous treatment: Abiraterone, Docetaxel, oral Cyclophosphamide, Cabazitaxel, Enzalutamide
- No visceral or lymph nodes metastasis
- PSA=22 Testosterone<0,03 ALP=247 LDH=386 CEA=2,0
Hb=13,6 Leucocytes=4450 Platelets=145000
No renal or hepatic dysfunctions

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- Previous treatment: Abiraterone, Docetaxel, oral Cyclophosphamide, Cabazitaxel, Enzalutamide
- No visceral or lymph nodes metastasis
- PSA=22 Testosterone<0,03 ALP=247 LDH=386 CEA=2,0
Hb=13,6 Leucocytes=4450 Platelets=145000
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Treatment??

- Symptomatic castration resistant prostate cancer metastatic to the bones, ECOG=1
- Previous treatment: Abiraterone, Docetaxel, oral Cyclophosphamide, Cabazitaxel, Enzalutamide
- No visceral or lymph nodes metastasis
- PSA=22 Testosterone<0,03 ALP=247 LDH=386 CEA=2,0
Hb=13,6 Leucocytes=4450 Platelets=145000
No renal or hepatic dysfunctions

Treatment → Referred to Radium-223 Treatment



- Is it necessary to perform more sensitive imaging evaluation to exclude visceral / lymph node metastasis before the indication of Radium-223?
- For baseline (pre treatment) bone evaluation what is the imaging method of choice?

- Initiated on Radium-223 on February 2017
PSA=22 / ALP=247 / LDH=386
- 17/02/2017: Cycle 1 Rad-223
PSA=18 ALP=101 LDH=226 – weaning of opioids
- 07/04/2017: Cycle 2 Rad-223
PSA=12 ALP=93 LDH=178
- 12/05/2017: Cycle 3 Rad-223
PSA=29 ALP=79 LDH=165



Clinical Case 1 - Discussion

- How frequent should we perform imaging to exclude visceral / lymph node progression during Radium-223 treatment?
- Is it necessary to re-evaluate bone metastasis with imaging methods during Radium-223 treatment?



- 17/02/2017: Cycle 1 Rad-223
PSA=18 ALP=101 LDH=226 – weaning of opioids
- 07/04/2017: Cycle 2 Rad-223
PSA=12 ALP=93 LDH=178
- 12/05/2017: Cycle 3 Rad-223
PSA=29 ALP=79 LDH=165
- After cycle 3: CT scans of thorax, abdomen and pelvis with no visceral or lymph node progression



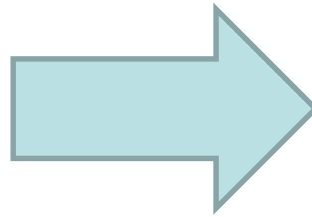
- 16/06/2017: Cycle 4 Rad-223
PSA=9,1 ALP=68 LDH=120
- 21/07/2017: Cycle 5 Rad-223
PSA=8,0 ALP=65 LDH=118
- 25/08/2017: Cycle 6 Rad-223
PSA=9,5 ALP=64 LDH=168
- No hematologic toxicity during the treatment
- Early pain response after cycle 1, with opioids weaning



Clinical Case – Bone Scan



January 2017



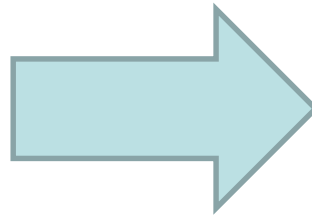
September 2017



Clinical Case – Bone Scan



January 2017



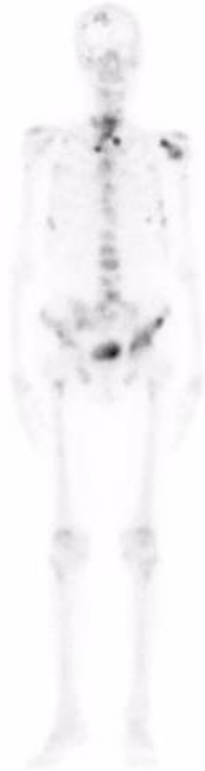
September 2017



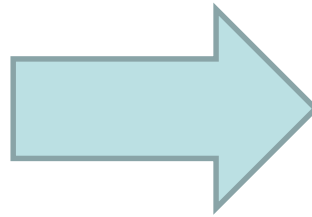
- After 6 cycles of Radium-223 patient stayed on follow up, with no active treatment, with normal life (very good quality of life)
- On January 2018 bone scan with no signs of progression, no visceral disease.
- PSA=9,9 ALP=103 LDH=174
- He is now 84 years old. And counting...



Clinical Case – Bone Scan



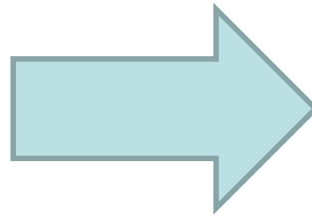
September 2017



January 2018



Clinical Case – Bone Scan



- What is the ideal timing for response evaluation after Radium-223?
- Could this patient be re-treated with Radium-223 in the future?

- TK, 86 years old now, asian
- Comorbidities: former-smoker (70 pack-year)
- 2010: Adenocarcinoma of the Prostate, Gleason 8 (4+4) PSA = 50ng/ml
cT3aN0M0
- 10/2010: Goserelin
- 01/2011 to 02/2011: Radiotherapy
- 07/2011: Nadir PSA = 0,043
- Continued on ADT – planning of 2 to 3 years



- 05/2012: Biochemical recurrence PSA = 3,8ng/ml Test = 27
No evidence of metastasis – M0
Association of bicalutamide to goserelin
- 08/2012: PSA = 0,85ng/ml
- 02/2013: PSA=4,9 – Still M0 – Asymptomatic
Interrupted Bicalutamide – Keep on ADT
- 07/2014: PSA=19,0 + Radiological progression to the bones

- 07/2014: PSA=19,0 + Radiological progression to the bones
- Started on Abiraterone + prednisone + zoledronic acid
- 10/2014: PSA=0,40
- 05/2015: PSA=4,9 – No radiological or clinical progression
- 09/2015: PSA=27 – No radiological or clinical progression
- 03/2016: PSA=66 – Radiological progression on the bones
- Asymptomatic



Bone Scan – 03/2016





- 03/2016: PSA=66 – Radiological progression on the bones
- Asymptomatic
- Didn't want IV chemo – wanted to fish...
- Started on oral cyclophosphamide

- 05/2016: PSA=24

- 10/2016: PSA=38

- 01/2017: PSA=50 – Radiological progression on the bones
- Asymptomatic







TERIOR FOTO1



POSTERIOR 12.01.2017



POSTERIOR 22.07.2016



POSTERIOR 15.01.2016



POSTERIOR 01.09.2015



TERIOR FOTO1



POSTERIOR 12.01.2017



POSTERIOR 22.07.2016



POSTERIOR 15.01.2016



POSTERIOR 01.09.2015

- Would you start Radium-223 in this asymptomatic patient at this time point?
- Do you feel comfortable to extrapolate the results of ALSYMPCA to asymptomatic patients?

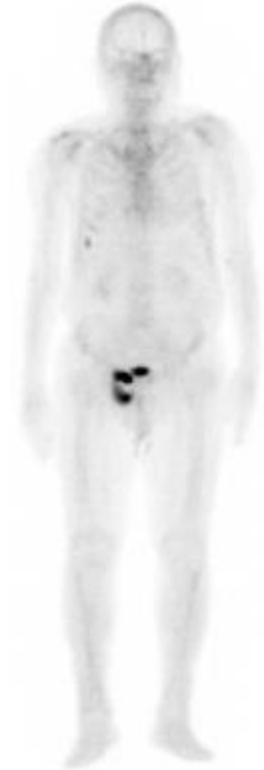
- 01/2017: PSA=50 – Radiological progression on the bones, asymptomatic
- 02/2017: Enzalutamide
- 05/2017: PSA=124 + Radiological progression to the bones
- Clinical progression: pain in the right hip and right leg (tibia)
- Couldn't fish anymore
- No visceral or lymph node metastasis
- No evident lesion on the prostate



RIOR FOTO2



05/2017



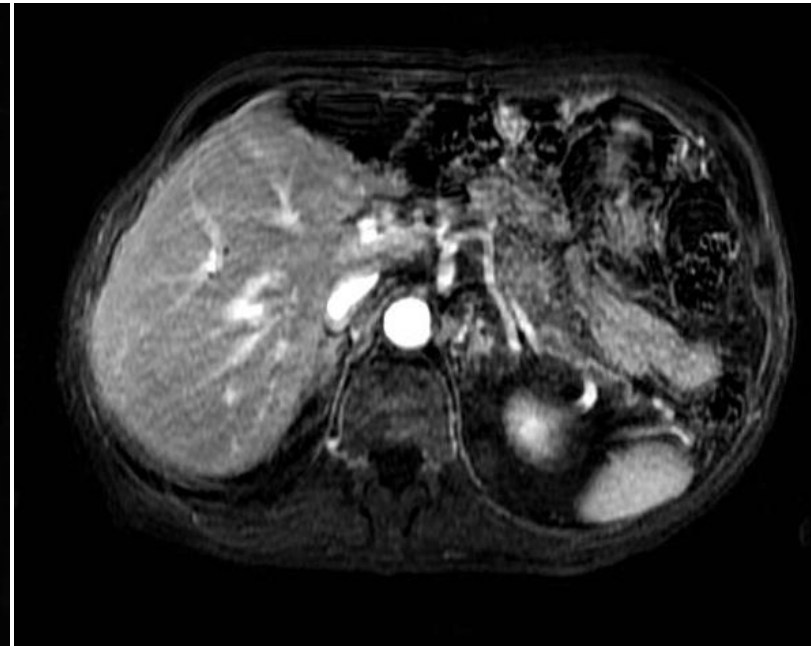
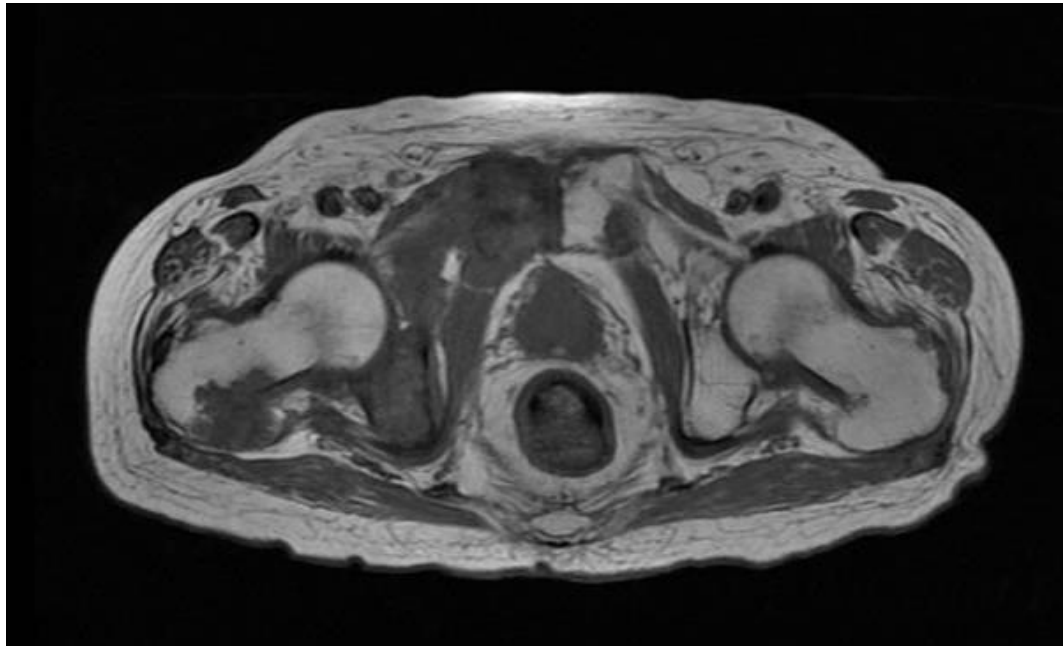


ERIOR FOTO2



05/2017









- 05/2017: PSA=124 + Radiological progression to the bones
- Clinical progression: pain in the right hip and right leg
- Morphine 30 mg/day
- No local disease, no lymph node or visceral metastasis

- Treatment ?

- 05/2017: PSA=124 + Radiological progression to the bones
- Clinical progression: pain in the right hip and right leg
- Morphine 30 mg/day
- No local disease, no lymph node or visceral metastasis

- Treatment → Referred to Radium-223

- Referred to radiation-oncology – discuss indication of radiotherapy in the symptomatic lesions (right tibia and right hip)



Clinical Case 2 - Discussion

- Would you indicate external radiotherapy concurrent with Radium-223 in this patient?

- Aside from this patient, do you feel comfortable to perform external radiotherapy concurrent with Radium-223?

- 05/2017: PSA=124 ALP=152 LDH=348 (ULN 480)
- 06/2017: Cycle 1 Radium-223
- 07/2017: Cycle 2 Radium-223
- 08/2017: -> After 2 cycles of Radium-223
PSA=164 ALP=133 LDH=319
- Pain response after 2 cycles – weaning of opioids
- Radiation oncology evaluation: contra indicated due to early pain response to Radium-223



- 08/2017: Cycle 3 Radium-223
PSA=179 ALP=135 LDH=315
- 09/2017: Cycle 4 Radium-223
PSA=246 ALP= 126 LDH=330
Maintaining clinical benefit – no pain at all

- 08/2017: Cycle 3 Radium-223
PSA=179 ALP=135 LDH=315
- 09/2017: Cycle 4 Radium-223
PSA=246 ALP= 126 LDH=330
Maintaining clinical benefit – no pain at all
- 10/2017: Cycle 5 Radium-223
PSA=231 ALP=146 LDH=287
- 11/2017: Cycle 6 Radium-223
PSA=205 ALP=158 LDH=280

- GI diarrhea, no hematologic toxicity, no other toxicities
- 01/2018:
- PSA=120 ALP=127 LDH=280
- No active treatment
- No pain
- Good quality of life
- Fishing again
- Waiting for response evaluation imaging



Obrigado pela atenção

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BACKUP CASE

- LS, 56 years-old, Engineer
- No comorbidities

- January 2015: back pain

- August 2015:
 - MRI and bone scan with multiple bone lesions
 - Biopsy of the prostate: Adenocarcinoma gleason 4+4
 - PSA=1504
 - No lymph node or visceral metastasis

- Adenocarcinoma of the prostate cT2aN0M1
- High volume disease



Clinical Case 3 – Bone Scan

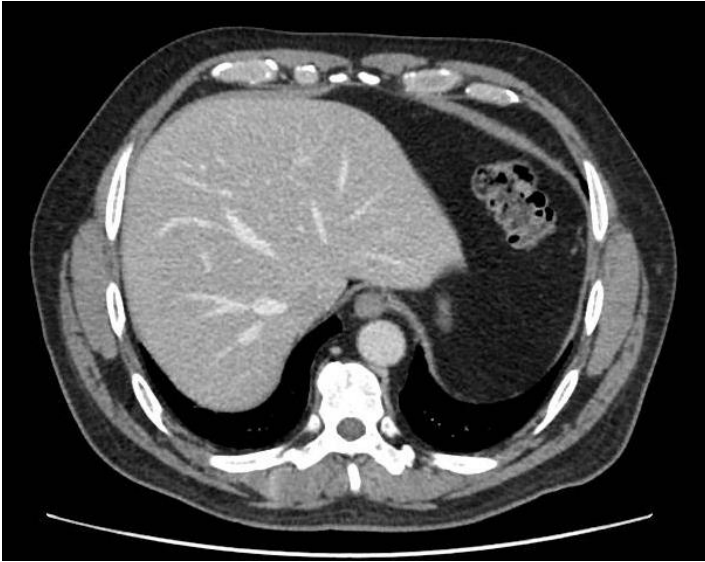


- Adenocarcinoma of the prostate gleason 8, cT2aN0M1
- High volume disease
- September 2015: Goserelin
- Docetaxel x 6 cycles from september/2015 to january/2016
- April/2016 → PSA=20,0 – no back pain anymore
- February/2017 → Nadir PSA=5,0

- 02/2017: PSA=5,0
- 06/2017: PSA=6,6 – No clinical or radiological progression
- 09/2017: PSA=8,5 – No clinical or radiological progression
- 01/2018: PSA=9,9
- Back pain requiring codein 3 times a week



Clinical Case 3 – CT Scans



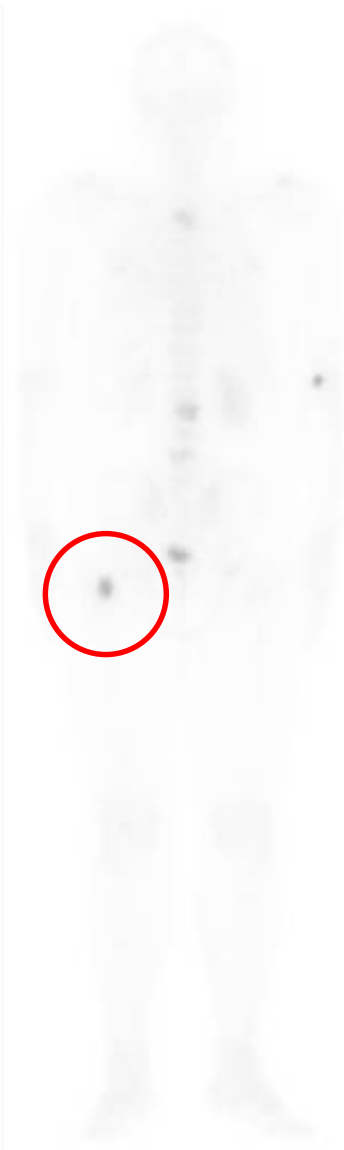


Clinical Case 3 – Bone Scan





Clinical Case 3 – Bone Scan



- Castration resistant prostate cancer with bone metastasis post
Charted
- 01/2018: PSA=9,9 ALP=62 LDH=271 (ULN 350)
- Back pain requiring codein 3 times a week
- Imaging with no visceral or lymph node metastasis, no evident
lesion on the propstate, 1 new lesion (proximal femur) on bone scan
- Treatment?



- Castration resistant prostate cancer with bone metastasis post Castrated
- 01/2018: PSA=9,9 ALP=62 LDH=271 (ULN 350)
- Back pain requiring codein 3 times a week
- Imaging with no visceral or lymph node metastasis, no evident lesion on the propstate, 1 new lesion (proximal femur) on bone scan
- Treatment → Referred to Radium 223 treatment

- What is the optimal timing of Radium-223 treatment?
- Who is the ideal candidate to Radium-223 treatment?



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