EAU- AUA updates
prostate cancer

ALI SALLOUM MD
FEBU
GENOMIC

- It is all about timing

- With genomic study we can predict the outcome of the disease and the best time for treatment

- Molecular feature will determine the speed of transition.

- P53 and PTEN

- Inactivation of the genes will cause increase in the tumor size and the behavior becomes more aggressive toward metastasis
• Tumor speed = molecular age \times \text{quantity} accelerator gene to the power quality accelerator genes

• The higher the nb of variation the higher the speed of growth and aggressiveness of the disease
• In conclusion in the future we will create a molecular speedometer for each patient in order to precisely predict individual patient progress
MP-MRI
• Is there a role for MRI and for what cost?

• the NPV of MRI in prostate cancer that was shown in many studies ranges between 63 -95%
Role of pre biopsy MRI

- Detection of csPC
- Rule out csPC
- Replace screening biopsies with few targeted cores using MRI TRUS image fusion
Detection of cs PC

- Baco et al 2015 and tontilla et al 2016 showed no benefit on cancer detection rate in biopsy naïve patients but 2 core MRI/TRUS TB was comparable to 12 core PB in detection local significant prostate cancer
Detection of cs PC

- In previously bx patient several studies showed the imp of MRI and the rate of detection of overall Pc was 42% and CSPC is 81%.

- The rate of detection was strictly correlated to the PIRAD scale on MRI.
AS

- MRI TRUS reclassify 10-33% of patients who met the criteria for AS

- The take home message that the selection should be based on systematic and MRI TRUS guided bx
BCR post EBRT

- MRI can detect and localize prostate cancer

- 79% was the detection rate on MRI trus bx morgan et al and rude et al
Rule out CS PC

- Le et al showed that 10-20% of CS PC still invisible on MRI

- So in case of negative MRI and Cs PC the majority went toward systemic bx
To replace screening bx

- Targeted bx may miss the target in 5-20% of cases
- “Only” targeted bx should be addressed for patients having large volume disease
- showed that in case of positive mri and Cs prostate ca random and targeted bx should be done for better estimation of tumor burden (nassiri et al)
conclusion

- The greatest benefit of pre bx MRI is for patients had neg bx before

- The main role of pre-bx MRI is to detect clinically significant pc and localise index lesion
• NPV is highly depending on methodology and selection criteria

• Systemic prostate bx with targeted bx should be done during the first bx sessions
ESUR

- 25% of patients with PSA less than 10 have positive bx and the majority are clinically insignificant
radio

• MRI TRUS fusion targeted bx detect higher cs prostate ca in comparison to higher rate of non cs pc on systemic bx

• large study by grenabo showed TB significantly more effective with less cores than SB (40 and 20% resp)

• **PIRAD classification** was strongly correlated with the detection of cs pc (5: 100%; 4: 75%)
2 prospective randomized studies have been published in 2015 showed the superiority of targeted bx over Sbx and the authors recommend targeted bx in the bx naïve patients.

Another imp study showed that patient with elevated psa level and negative MRI can enter the protocol of active surveillance rather than immediate bx as the NPV was 95%.
Conclusion

- MRI TRUS fusion bx detects more significant pc with less cores and decrease the detection rate of low risk pca

- MRI can avoid unnecessary bx in a high nb of men

- MRI should be part of screening tools for prostate ca but the cost can be an obstacle for some health system and biparametric MRI is the solution
guidelines

• Multiparametric magnetic resonance imaging (mpMRI) has excellent sensitivity for the detection and localisation of Gleason score > 7 cancers

• Before repeat biopsy, perform mpMRI when clinical suspicion of PCa persists in spite of negative biopsies. Lev 1
ART VS ESRT
ART

- PNo: 3 randomized trial showed clear advantage for ART concerning the OS

- EORTC 22911 study included patient with R1 and it showed clear advantage in favor of biochemical progression FS rate and of OS but not significant

- German randomized prospective trial showed BPFS is better by 20% in favor ART
• And with ART the recurrence came down for 50\% on patient with R1

• surgical margin is independent predictive factor
• PN+: ART showed sig imp in cancer specific mortality in combination with ADT. (Mayo clinic trial)
Combination of ART and ADT

- High gleasons core represents the only predictor of early biochemical recurrence after RP and ART in patients with PT3No
**conclusion**

- Clear evidence in favor of ART in patients having PT3No
- Most profit are patients having R1, large SM, or multiple
- No overtreatment for patient with PT3 high gleason score
- LE 2b for pN+
- Low rate side effect
Cons ART

- 3 studies SWOG, EORTC and ARO showed the advantage of ART and depending on these studies the AUA guidelines recommend ART for patients having R1, EPE, SVI.

- 50% of men after RP will have adverse pathology but 50% recurr

- 33% of RP will have BCR but many of them do not recurr

- 10% utilization of ART in the states
These 3 studies have weak points in the randomization of patients, the percentage of patients that were included and having low gleason score.

The high rate of urinary problem after RT and some of them were very difficult to manage.
• Adj RT increase the risk of UI by 1.6

• Minimal difference between SRT and ART in some studies

• ART increase also the rate nonurological problem and procedures
• Recent retrospective studies showed that ESRT has comparable results in addition that significant nb of patient may avoid RT
• Conclusion: high level evidence pending on ART vs ESRT

• The current evidence on RT is weak

• ESRT similar survival improvement but less exposure
Guidelines

- In patients with pT3, NoMo PCa and an undetectable PSA following RP, discuss adjuvant EBRT because it at least improves BFS.

- Inform patients with pT3, NoMo PCa and an undetectable PSA following RP about salvage irradiation as an alternative to adjuvant irradiation when PSA increases.
Chemo and hormonal

- CHAARTED trial
- GETUG 15 trial (no prednisone)
- Both of them is to compare docetaxel vs ADT plus doc in hormone naive metastatic pca
• GETUG study showed no advantage in OS
• Chaartered one showed sig imp in overall survival
• STAMPEDE: includes metastatic patients or high risk patients (T3 T4, psa>40, GL>=8)

• Outcome measures : OS and FFS

• Different arms : SOC
  SOC plus zoledro acid
  SOC plus docetaxel
  SOC plus DOC plus ZOLEDRO acid
• DOC with ADT improves the progression free survival and OS in patients with N+ and M1

• Conclusion was: doc improves survival for hormone naïve prostate ca and it should be considered in suitable men with newly dg MPC and for selected high risk non metastatic disease in view of prolongation of FFS
Metanalysis of aggregate data (GETUG15, STAMPEDE and CHAARTED) showed in M1 patient we have clear benefit in OS and FFS
guidelines

- In newly diagnosed M1 patients, offer castration combined with docetaxel, provided patients are fit enough to receive chemotherapy. (1a)
Prevent and management of prostate biopsy complications

- Infection related complication dramatically increased in the last years in many countries.

- TRUS is low invasive procedure but highly associated with infection complications

- The guidelines recommend fluoroquinolone as prophylactic antibiotic before TRU BX
Infectious complication is correlated to the triad patient, pathogen and antibiotic.

ESBL prevalence is dramatically increased and studies showed it is the main cause of urosepsis post bx.

Epidemiological data is not respecting in the guidelines.
Patient selection should not be unique. Patients having risk factors are more vulnerable to esbl UTI post BX.
New strategy

- Risk assessment for selecting patients
- Microbiological evaluation of the fecal flora
- Change biopsy route
- Alternative molecule with enhanced susceptibility (fosfomycin??)
- Decrease number of biopsy cores
Castrate resistant status

Ensure that testosterone levels are confirmed as < 50 ng/mL, before diagnosing CRPC.

Do not treat patients for non-metastatic CRPC outside of a clinical trial.

Counsel, manage and treat patients with mCRPC in a multidisciplinary team.

In men treated with maximal androgen blockade, stop anti-androgen therapy once PSA progression is documented.
Comment: Four to six weeks after discontinuation of flutamide or bicalutamide, an eventual anti-androgen withdrawal effect will be apparent.

Treat patients with mCRPC with life prolonging agents. Base the choice of first line treatment on the performance status, symptoms, comorbidities and extent of disease (alphabetical order: abiraterone, docetaxel, enzalutamide, radium-223, sipuleucel-T).

Offer patients with mCRPC who are candidates for cytotoxic therapy docetaxel with 75 mg/m2 every 3 weeks.

In patients with mCRPC and progression following docetaxel chemotherapy, offer further life-prolonging treatment options, which include cabazitaxel, abiraterone, enzalutamide and radium-223.

Offer bone protective agents to patients with skeletal metastases to prevent osseous complications.
However, the benefits must be balanced against the toxicity of these agents, and jaw necrosis, in particular, must be avoided.

Offer calcium and vitamin D supplementation when prescribing either denosumab or bisphosphonates.

Treat painful bone metastases early on with palliative measures such as EBRT, radionuclides, and adequate use of analgesics.

In patients with spinal cord compression, start immediate high-dose corticosteroids and assess for spinal surgery followed by irradiation. Offer radiation therapy alone if surgery is not appropriate.