İSTANBUL MEDENİYET ÜNİVERSİTESİ

GÖZTEPE EĞİTİM ve ARAŞTIRMA HASTANESİ ÜROLOJİ

EAU19 BARCELONA 15-19 March 2019

eau European Association of Urology

# Avrupa Üroloji Kongresinden İzlenimler

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İstanbul Medeniyet Üniversitesi

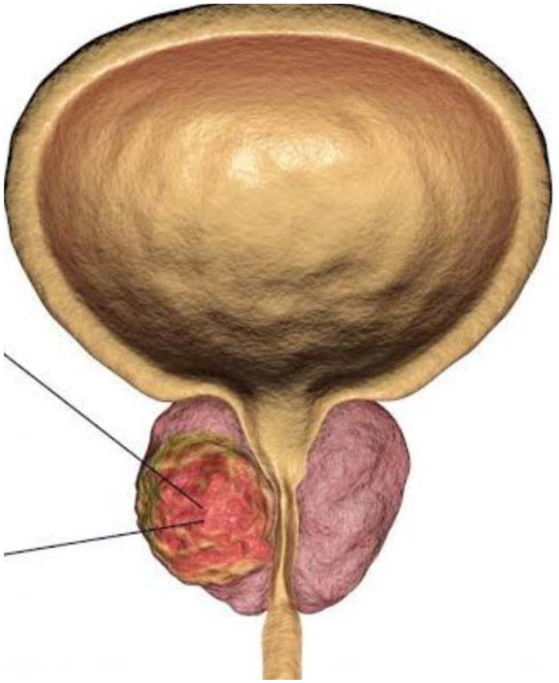
tr esru ESRU Türkiye

# Prostat Kanseri Markerlar

A. Tedavi seçiminde

A. Hastalık riskini belirlemede

A. Tanıda ve Aktif izlem Hastalarının seçiminde



372

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# Comparative proteome analysis identified NAMPT as a potential serum marker for the prediction of docetaxel-resistance in prostate cancer

Keresztes D. [1], Módos O. [1], Szűcs M. [1], Hüttl A. [1], Csizmarik A. [1], Nagy N. [1], Kretz V. [1], Bracht T. [2], Sitek B. [2], Witzke K. [2], Puhr M. [3], Sevcenko S. [4], Kramer G. [5], Shariat S. [5], Nyirády P. [1], Szarvas T. [1,6]

[1]Semmelweis University, Dept. of Urology, Budapest, Hungary, [2]Ruhr University Bochum, Medizinisches Proteom-Center, Bochum, Germany, [3]Medical University of Innsbruck, Dept. of Urology, Innsbruck, Austria, [4]Donauspital, Dept. of Urology, Vienna, Austria, [5]Medical University of Vienna, Dept. of Urology, Vienna, Austria, [6]University Hospital Essen, University of Duisburg-Essen, Dept. of Urology, Essen, Germany

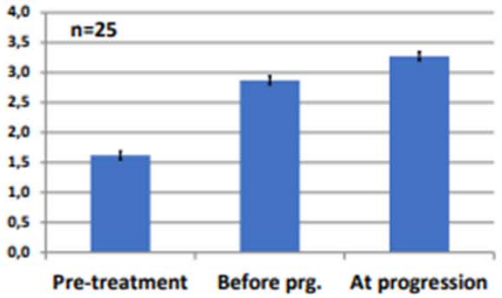



***Figure 3. Mean NAMPT serum levels (ng/ml)***
*Significantly increased NAMPT serum levels were detected before and at radiographic progression.*

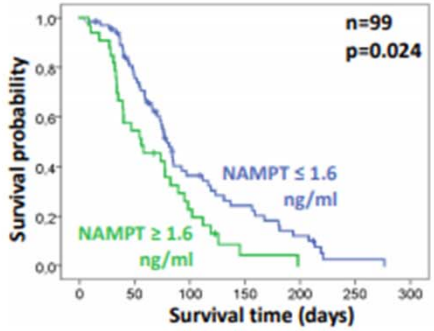



***Figure 4. Kaplan-Meier Plot***
*High NAMPT serum levels were associated with poor patients' survival in DOC-treated CRPC patients.*

99 hasta çalışmaya dahil edilmiş.

NAMPT (Vistatin) Dosetaksel ile tedavi edilen CRPC hastalarında sağkalım ve progresyon ile ilişkili bulunmuş.

Bu hastalarda enzalutamid/abireteron kullanılabilir.

**369: Tissue specific NKX3.1 positive circulating tumor cells isolated by ISET in prostatic cancer patients** EAU19 16-03-2019

**Authors:** Monterisi S. [1], Colombo P. [2], Duga S. [3], Saita A. [4], Elefante M.G. [2], Casale P. [4], Buffi N.M. [4], Hurle R. [4], Lunghezzani G. [4], Guazzoni G. [4], Veronesi G. [5], Lazzeri M. [4]

**Institutes:** [1] Humanitas Clinical and Research Center, Lab. Medical Genetics and RNA Biology, Rozzano, Italy, ...

28 hasta çalışmaya dahil edilmiş.
Radikal prostatektomi yapılan 3 hastanın 2sinde DHT +
Bu iki hastada metastaz gelişmiş.
Gleason 5+5 AdenoCa saptanan bir hastada DHT+
Gleason 3+3 tümörlerde DHT -

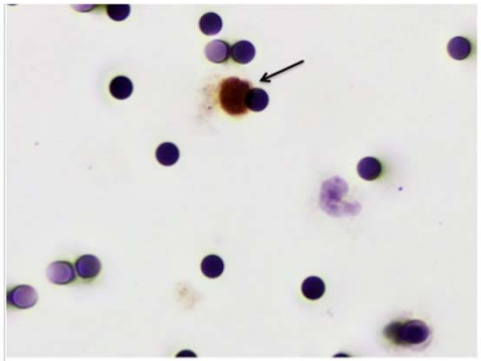


Fig.1: Rappresentative image of a NKX3.1 cell (black arrow) and a blood cell (hematoxylin staining) identified among filter-retained cells from the blood of a advanced prostate cancer patient.

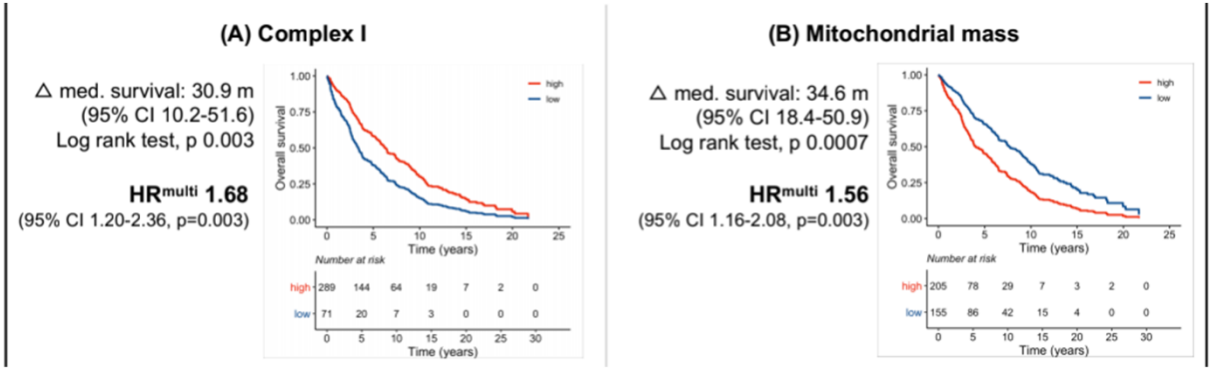
# Mitochondrial dysfunction correlates directly with progression and poor long-term prognosis in prostate cancer

*Ashwin Sachdeva[1,2,4], Claire Hart[4], Christopher Carey[3], Conor Lawless[1], Mick Brown[4], Laura Greaves[1], Rakesh Heer[2], Doug Turnbull[2], Noel Clarke[4]*

*1. Wellcome Centre for Mitochondrial Research, 2. Northern Institute for Cancer Research, 3. Molecular Pathology Node, Newcastle University, Newcastle-upon-Tyne, United Kingdom*
*4. Genito-urinary cancer research group, Christie Hospital, Manchester, United Kingdom.* ashwin.sachdeva@gmail.com

Warburg shift tümör hücrelerinin,

Mitokondride yaptıkları oksidatif fosforilasyon yerine hızlı enerji elde etmek amacıyla glikolizi tercih etmeleridir.




Mitokondriyel disfonksiyon agresif prostat kanseri ile ilişkilidir. Progresyon için erken bir marker olarak kullanılabilir.

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**External validation of SelectMDx in an opportunistic screening cohort in first TRUS-guided biopsy without MRI imaging**

**CONCLUSIONS**

1. **SelectMDx offered us a moderate discrimination ability, but with valuable clinical utility in clinical scenarios of low expected prevalence of GG≥2**
2. **In Centers with no easy and reliable availability for MRI before first Bx, it could be a useful tool to avoid around 40% of initial Bx in men with PSA between 3-10 ng/mL**

İlk biyopsiden önce PSA 3-10 arası hastalarda

Klinik önemli prostat kanserini

PCA3 and ERSPC and PBCG risk skorlarına göre daha iyi analiz edebiliyor.

%40 gereksiz biyopsiyi önlüyor. MR güvenilir ve erişilebilir değilse.

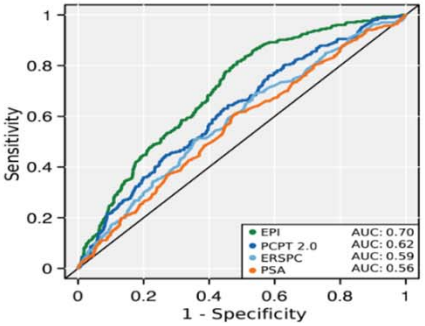
# Pooled analysis of >1000 patients enrolled in two independent prospective validation studies show consistent performance of a urine exosome gene expression assay to rule-out benign and low-grade prostate cancer at initial biopsy

Noerholm M.[1], McKiernan J.[2], Donovan M.J.[3], Partin A.[4], Carter B.[4], Brown G.[5], Margolis E.[6], Torkler P.[1], Skog J.[7], Shore N.[8], Andriole G.[9], Thompson I.[10], Carroll P.[11]

(1) Exosome Diagnostics GmbH, Martinsried, Germany, (2) Columbia University Medical Center, Dept. of Urology, New York, USA, (3) Icahn School of Medicine at Mt. Sinai, Dept. of Pathology, New York, USA, (4) Johns Hopkins Hospital, Dept. of Urology, Baltimore, USA, (5) Delaware Valley Urology, Vorhees, United States of America, (6) Urology Center of Englewood, Englewood, USA, (7) Exosome Diagnostics, Waltham, USA, (8) Atlantic Urology Clinics, Myrtle Beach, USA, (9) Washington University, Dept. of Surgery, Saint Louis, USA, (10) UT Health Science Center, San Antonio, USA, (11) University of California, Dept. of Urology, San Francisco, USA

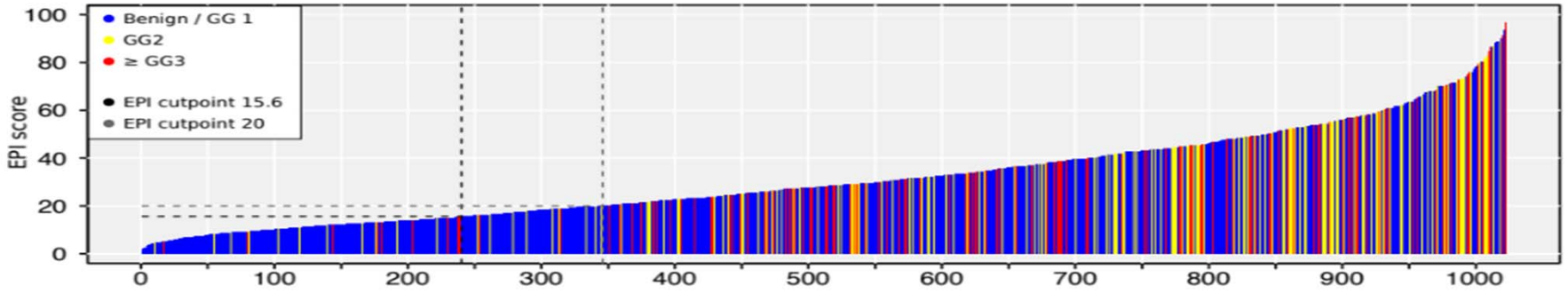
**Table 2: Demographics & Performance**

| | | |
|---|---|---|
| **Cohort Size** | 1022 | |
| **Age (Median)** | 63 years | |
| **PSA (Median)** | 5.3 ng/mL | |
| **African American** | 15.5% | |
| **Familyhistory - Yes** | 18.5% | |
| **EPI Cutpoint** | Validated (15.6) | Alternative (20) |
| **Prevalence HGPCa** | 29.9% | 29.9% |
| **Biopsies Avoided** | 23.4% | 33.8% |
| **Sensitivity** | 92.5% | 88.2% |
| **Specificity** | 30.2% | 43.2% |
| **NPV** | 90.4% | 89.6% |




EPI is a non-invasive, easy to use, world's first exosome based 3-gene expression urine assay, which:

- discriminates high-grade (≥GG2) from low-grade (GG1) PCa and benign disease
- accurately identifies patients with higher grade disease
- reduces the total number of unnecessary biopsies



# 547: Prostate MRI, with or without targeted biopsy and standard biopsy for detecting prostate cancer: A Cochrane systematic review and meta-analysis

EAU19
16-03-2019

1 1 2 2 3 2

**Table 1. Detecting GG ≥ 2 prostate cancer by MRI, MRI-targeted biopsy, MRI-pathway and standard biopsy**

| | |
|---|---|
| **Population:** | 10.810 men with a suspicion of prostate cancer (PSA or DRE based) undergoing their first or a repeat biopsy. |
| **Setting:** | First-biopsy setting, repeat-biopsy setting or a mixed setting |
| **Tests:** | MRI; MRI-targeted biopsy (MRI-TBx) in men with a positive MRI; the MRI-pathway (MRI with or without MRI-TBx); and standard biopsy (SBx) |
| **Reference test:** | Template-guided biopsy, which comprehensively samples all zones of the prostate (TemplBx) |

| Tests | Setting | N studies (patients) | Summary sensitivity (95% CI) | Summary specificity (95% CI) | Detection ratio (95% CI) | Implications in a population of 1000 men* | Risk of bias: patient selection & reference standard domain | Risk of bias: other domains |
|---|---|---|---|---|---|---|---|---|
| **MRI** | Mixed | 10 (2719) | 0.90 (0.81-0.95) | 0.38 (0.30-0.47) | n.a. | csPCa will be missed in 30 men | moderate to high | low |
| **MRI-TBx** | Mixed | 6 (1288) | 0.83 (0.74-0.90) | 0.92 (0.88-0.94) | n.a. | csPCa will be missed in 51 men | moderate to high | low |
| **MRI-pathway** | Mixed | 6 (1885) | 0.74 (0.63-0.82) | 0.95 (0.93-0.97) | n.a. | csPCa will be missed in 78 men | moderate to high | low |
| **SBx** | Mixed | 4 (3421) | 0.65 (0.22-0.93) | 1.00 (0.97-1.00) | n.a. | csPCa will be missed in 105 men | high | low |
| **MRI-pathway versus SBx** | First-Bx | 16 (2829) | n.a. | n.a. | 1.04 (0.91-1.19) | MRI-pathway and SBx detect an equal proportion of men with csPCa | moderate to high | low |
| | Repeat-Bx | 8 (1354) | n.a. | n.a. | 1.45 (1.12-1.87) | MRI-pathway detects a larger proportion of men with csPCa than SBx | moderate to high | low |

*assuming a pre-test probability of 30%; MRI = magnetic resonance imaging; MRI-TBx = MRI-targeted biopsy; MRI-pathway = MRI with or without targeted biopsy; SBx = standard systematic biopsy; TemplBx = Template-guided biopsy; csPca = clinically significant prostate cancer; GG = ISUP grade group; First-Bx = biopsy naive men; Repeat-Bx = men with a history of previous negative biopsy; n.a. = not applicable.

**Table 2. Detecting GG = 1 prostate cancer by MRI, MRI-targeted biopsy, MRI-pathway and standard biopsy**

| | |
|---|---|
| **Population:** | 8.164 men with a suspicion of prostate cancer (PSA or DRE based) undergoing their first or a repeat biopsy. |
| **Setting:** | First-biopsy setting, repeat-biopsy setting or a mixed setting |
| **Tests:** | MRI; MRI-targeted biopsy (MRI-TBx) in men with a positive MRI; the MRI-pathway (MRI with or without MRI-TBx); and standard biopsy (SBx) |
| **Reference test:** | Template-guided biopsy, which comprehensively samples all zones of the prostate (TemplBx) |

| Tests | Setting | N studies (patients) | Summary sensitivity (95% CI) | Summary specificity (95% CI) | Detection ratio (95% CI) | Implications in a population of 1000 men* | Risk of bias: patient selection & reference standard domain | Risk of bias: other domains |
|---|---|---|---|---|---|---|---|---|
| **MRI** | Mixed | 8 (1392) | 0.68 (0.56-0.78) | 0.27 (0.17-0.40) | n.a. | Potential overdiagnosis is avoided in 64 men | moderate to high | low |
| **MRI-TBx** | Mixed | 4 (396) | 0.52 (0.13-0.89) | 0.99 (0.67-1.00) | n.a. | Potential overdiagnosis is avoided in 96 men | moderate to high | low |
| **MRI-pathway** | Mixed | 4 (558) | 0.30 (0.15-0.51) | 0.99 (0.88-1.00) | n.a. | Potential overdiagnosis is avoided in 140 men | moderate to high | low |
| **SBx** | Mixed | 4 (3421) | n.p. | n.p. | n.a. | n.p. | n.a. | n.a. |
| **MRI-pathway versus SBx** | First-Bx | 13 (1689) | n.a. | n.a. | 0.65 (0.53-0.80) | MRI-pathway avoids more overdiagnosis and biosy procedures than SBx | moderate to high | low |
| | Repeat-Bx | 6 (992) | n.a. | n.a. | 0.54 (0.35–0.82) | MRI-pathway avoids more overdiagnosis and biosy procedures than SBx | moderate to high | low |

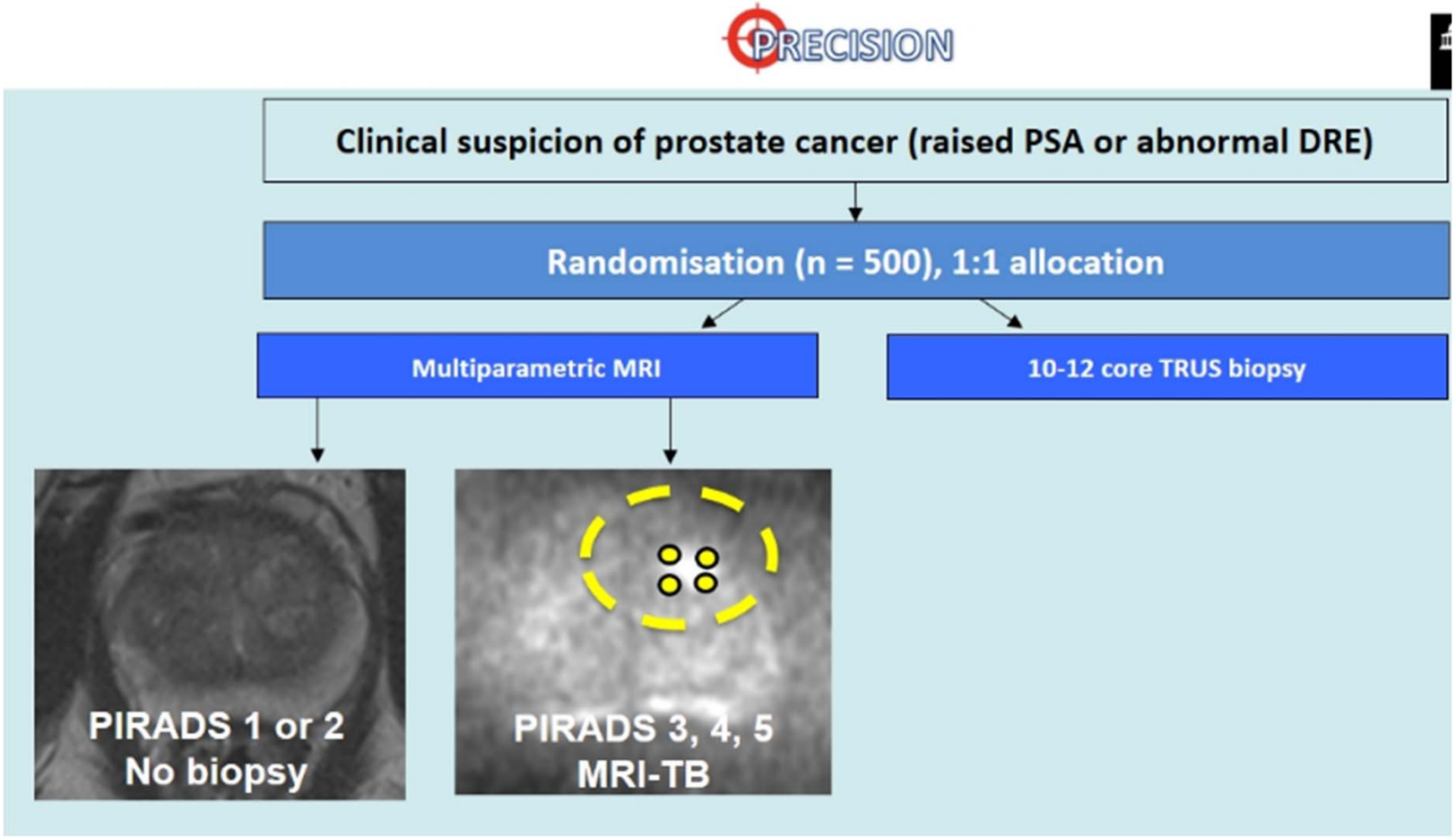
*assuming a pre-test probability of 20%; MRI = magnetic resonance imaging; MRI-TBx = MRI-targeted biopsy; MRI-pathway = MRI with or without targeted biopsy; SBx = standard systematic biopsy; TemplBx = Template-guided biopsy; First-Bx = biopsy naive men; Repeat-Bx = men with a history of previous negative biopsy; GG = ISUP grade group; n.a. = not applicable.

MRI pathway: %26 standart biyopsi %35 klinik önemli prostat kanseri kaçırırken

Gereksiz biyopsilerin %31’ ini önlerken

Gleason 3+3 lerin yakalanmasını %70 oranında engelliyor.

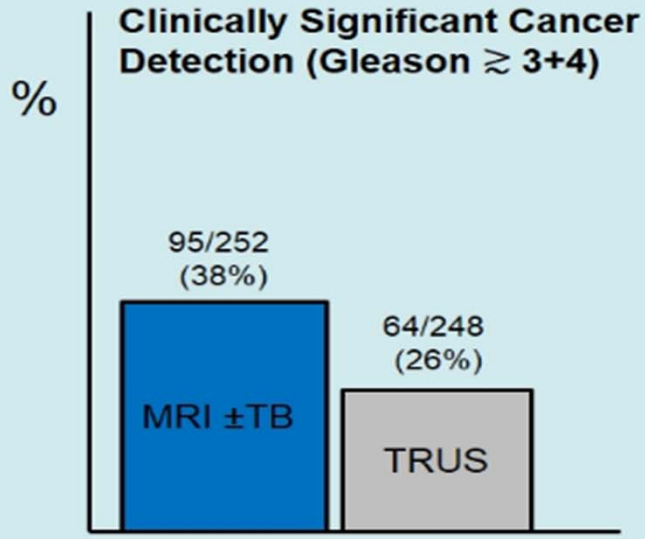
# Görüntüleme biyopsi sayısını azaltabilir mi?

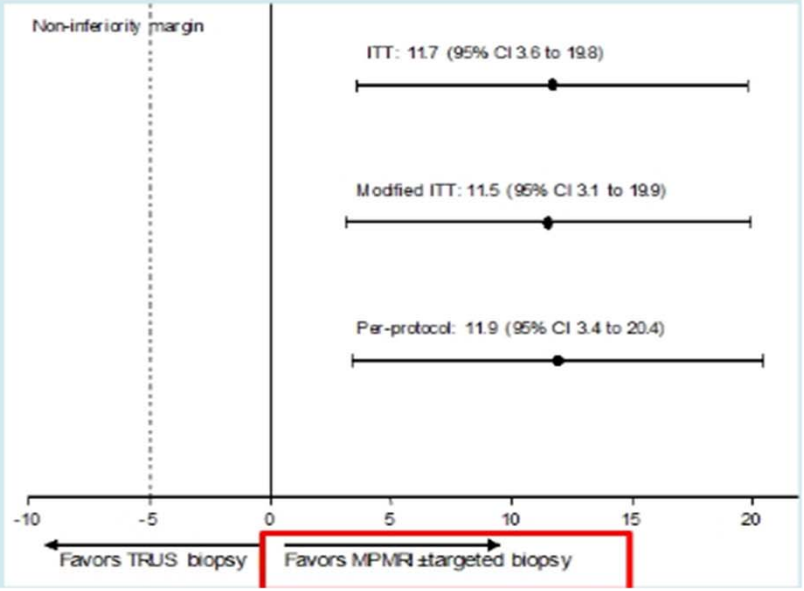


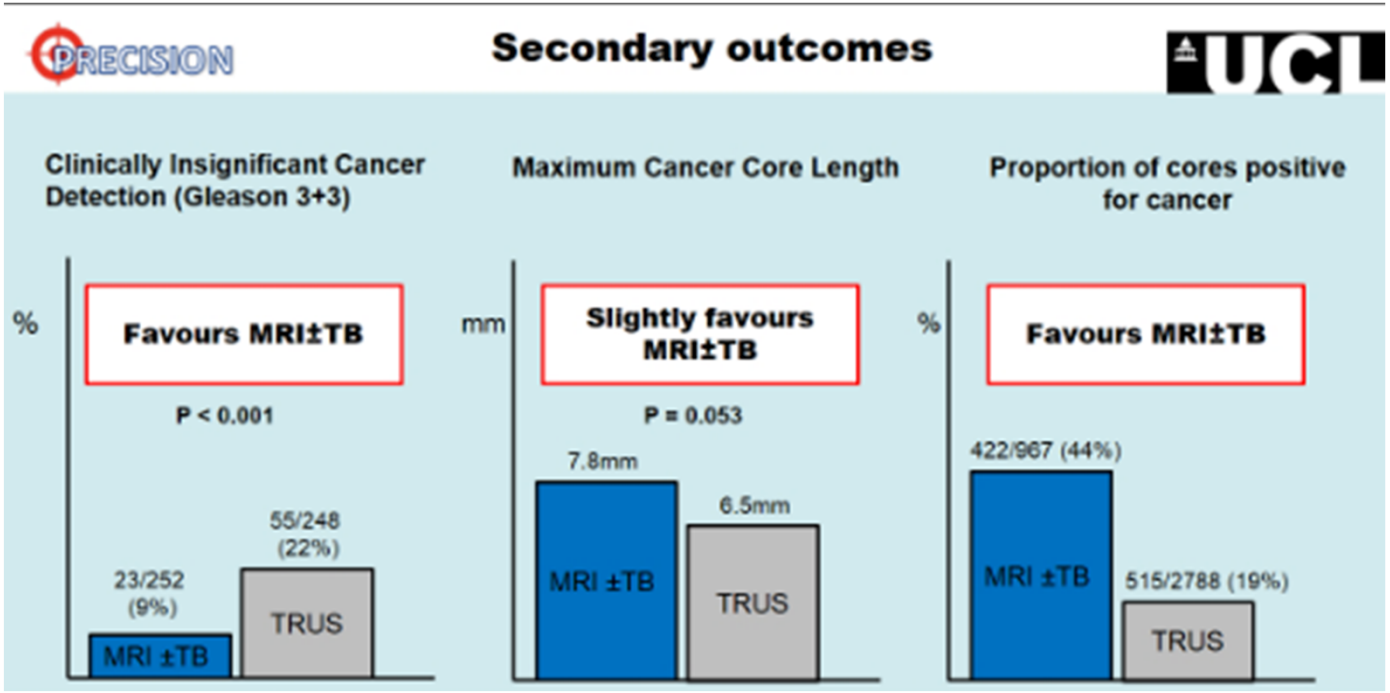
# Outcomes

**71/252 (28%) of men avoided biopsy in the MRI arm**

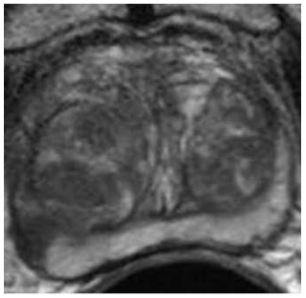
**Median 4 cores in MRI ±TB arm versus median 12 cores in TRUS biopsy arm**






Daha az biyopsi
Daha az overdiagnose
daha fazla klinik önemli prostat kanseri
PSAD>15 ise yakın takip!



%95 e varan Negatif prediktif değer Gleason3+4 için

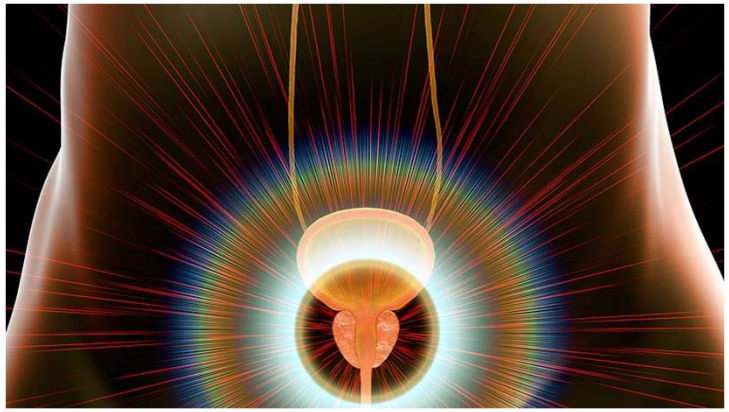
%30 gereksiz biyopsiyi önler

Daha az klinik önemsiz prostat kanseri saptar

| Recommendations for biopsy naïve patients | LE | Strength rating |
|---|---|---|
| Perform mpMRI before prostate biopsy. | 1a | Weak |
| When mpMRI is positive (PI-RADS ≥3), combine targeted and systematic biopsy. | 2a | Strong |
| When mpMRI is negative (PI-RADS ≤2) and clinical suspicion of prostate cancer is low, omit biopsy based on shared decision making with the patient. | 2a | Weak |

| Summary of evidence | LE | Strength rating |
|---|---|---|
| Systematic biopsy is an acceptable approach if mpMRI is unavailable. | 3 | Strong |

FAST MR



- Kontrastsız
- Biparametrik
- Dinamik görüntü hariç
- Mp MR= 16 dakika iken Fast 8 dakika
- %55 daha ucuz
- Klinik önemli prostat kanserini dışlamada kullanılabilir
- EUJ' da sonuçları yakında yayınlanacak.

I. Aktif İzlem
    A. Aİ sınırlarını genişletebilir miyiz?
    B. Görüntülemeler ve risk sınıflaması iyileştirilebilir mi?
II. Lokalize Prostat kanseri tedavisi
    A. PLND
III. İleri evre Hastalık
    A. Görüntü rehberli tedaviler
    B. Sitoredüktif RP

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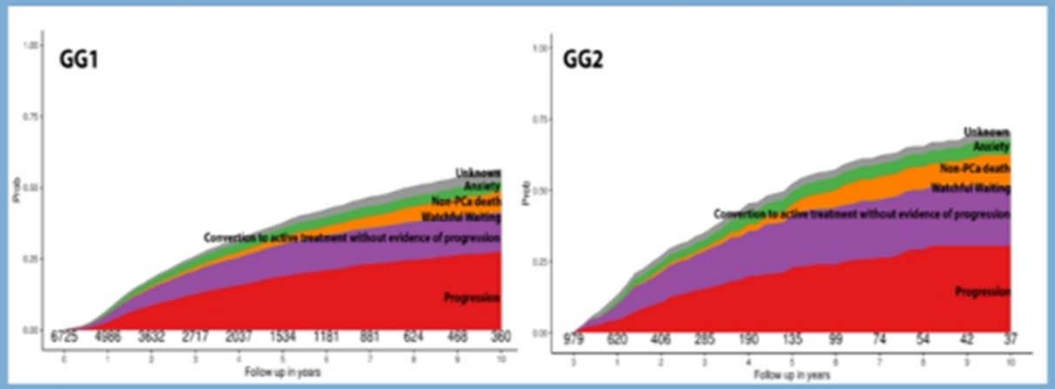
# EXPANDING ACTIVE SURVEILLANCE TO GLEASON 3+4?

## Results from the Movember GAP 3 Consortium

✓ 7,704 men on AS from 14 centres; 6,725 men with GG1 (87%) and 979 men with GG2 (13%)




**Discontinuation at 5:** 40% GG1 vs 50% GG2
**Reason for discontinuation:** GG2 switch to active treatment:
- Due to **progression** (19% vs **23%**)
- **Without evidence of progression:** (11% vs **18%**)

Adverse pathology : 34% GG1 vs 42% GG2

| Recommendations | Strength rating |
|---|---|
| **Active surveillance (AS)** | |
| Offer AS to highly selected patients (< 10% pattern 4) accepting the potential increased risk of further metastases. | Weak |

MR teknolojisi ve gen profilinin daha etkin kullanılması ise daha fazla Gleason 3+4 tümörün aktif izleme alınabilmesi olası olabilir.

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# ACTIVE SURVEILLANCE – PROGNOSTIC FACTORS

174 hasta çalışmaya dahil edilmiş.
ISUP önerilerine göre raporlanması gereken parametreler ve MR' da lezyon varlığı progresyon açısından karşılaştırılmış.
MR ve Başlangıçtaki PSA en önemli progresyon belirteçleri olarak belirlenmiş.

| Covariate | Multivariate Table | |
|---|---|---|
| | HR | p |
| MRI (Yes vs. No) | 0.31 | 0.003 |
| % Positive Cores per Side | 1.05 | 0.063 |
| % PCa In The Most Involved Core | 1.01 | 0.647 |
| Total Cores | 0.94 | 0.262 |
| Percentage of positive cores | 1.04 | 0.314 |
| PSA at diagnosis (ng/ml) | 1.18 | 0.006 |
| Age (yrs) | 0.99 | 0.763 |
| Clinical Stage (T2a vs T1) | 0.99 | 0.982 |

C-index unchanged (79%)

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# ACTIVE SURVEILLANCE – CAN WE AVOID REPEATED BIOPSY?

| Study | Methods | Results |
|---|---|---|
| Giganti F et al | 150 men with GG1 or 2 on AS | 12, 24 and 60 months Progression free survival for PRECISE 1-3, was 98-100% (radiological stability) |
| Von Beyme Cortés et al | 147 patients under AS with Gleason score of 3+3=6 or 3+4=7a were initially enrolled and received mp-MRI (n=55) | NPV was 100%. PPV was 64%. Sensitivity was 100% and specificity 59%. |
| Osses D.F. et al | 81 men underwent both an MRI±TBx at baseline and at confirmatory biopsy | Upgrading was detected in stable confirmatory MRIs in 35% of men. TBx missed upgrading in 43% detected by TRUS-Bx only |
| Fishelevitz A. et al | 71 men on AS with mpMRI prior to biopsies | Re-classification by systematic only in 40% of the cases |

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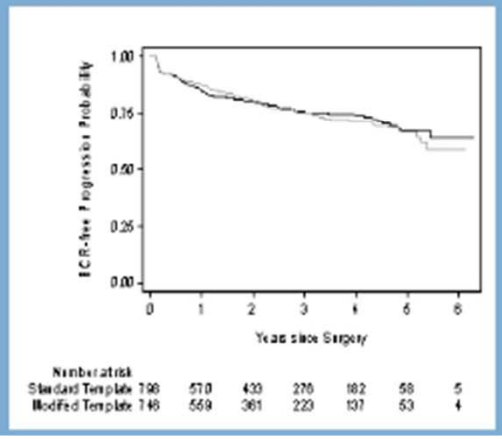
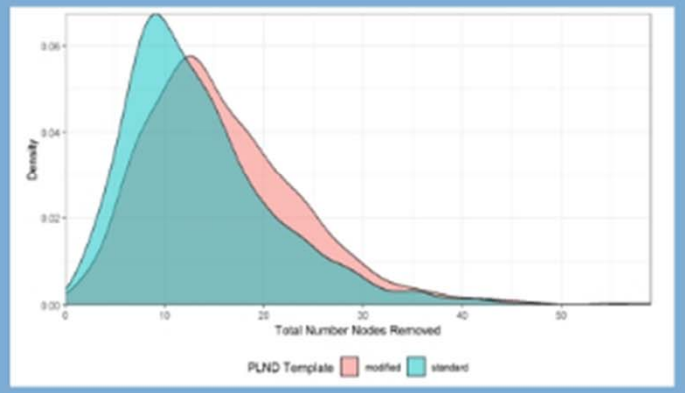
# Extended versus Standard Pelvic Lymph Node Dissection: Results of RCT

1480 hasta randomize ediliyor
Genişletilmiş LND: 757(obturator, external iliak, hipogastrik)
Sınırlı LND 723(obturator fossa)

EACH SURGEON WAS RANDOMIZED TO LIMITED VS EXTENDED PLND FOR A 3-MONTH PERIOD

Primary end-point: time to BCR




Same rates of Grade 2/3 complications: 12 vs 11%
No grade 4/5 complications

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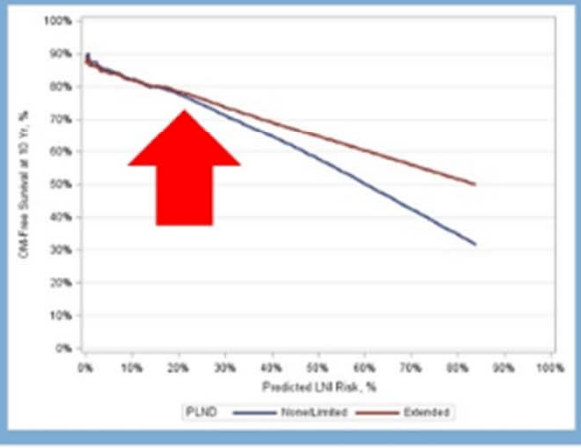
# Extended lymph node dissection is associated with improved OS in patients with very high-risk PCa

- ✓ Natiocal Cancer Data-Base: 406,409 patients
- ✓ Patients undergoing ePLND (HR=1.22) had 8% incrementally lower risk of 10-yr mortality as compared to patients undergoing none/limited PLND (HR=1.31) for every 10% increment in Godoy-nomogram predicted LNI risk (p<0.0001).

**CMF survival in patients at high risk of LNI according to the extent of LND**




Genişletilmiş LND yapılan hasta grubunda 10 yıllık takipte %8 daha az mortalite görülüyor.

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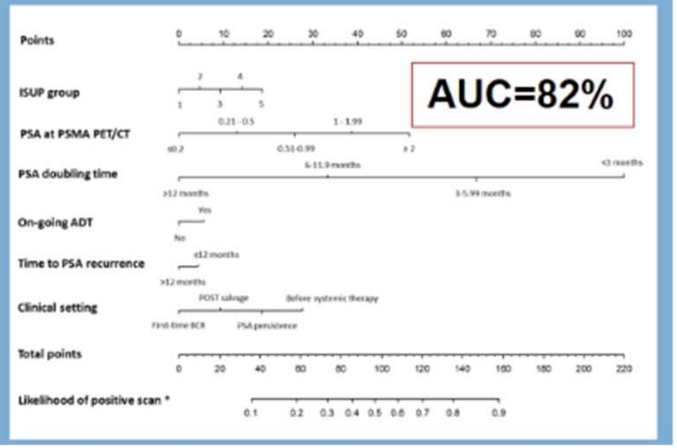
**Which patient with biochemical recurrence after primary treatment for prostate cancer would result in a positive $^{68}$Ga-PSMA PET/CT? A clinical tool to guide physicians before suggesting $^{68}$Ga-PSMA PET/CT**

- ✓ 703 PCa patients with confirmed biochemical recurrence (BCR)
- ✓ Patients were stratified according to different clinical settings of recurrence: first PSA relapse (detection rate: **40%**), BCR after salvage therapy (detection rate: **54%**), PSA persistence after primary therapy (detection rate: **60%**) and disease progression before starting systemic therapies (detection rate: **87%**).

2019 EAU Guidelines

| Prostate-specific antigen (PSA) recurrence after radical prostatectomy | LE | Strength rating |
|---|---|---|
| Perform PSMA PET/CT if the PSA level is > 0.2 ng/mL and if the results will influence subsequent treatment decisions. | 2b | Weak |




ISUP Grup
PSA
PSA DT
ADT
PSA rekürrensine kadar geçen süre
Klinik durum

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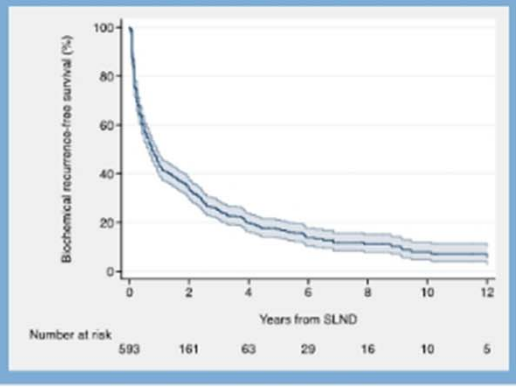
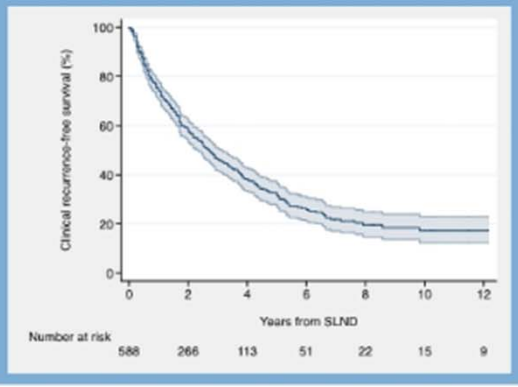
# LONG TERM OUTCOMES OF SALVAGE LND

Salvage LND sonuçları yüzgüldürücü değil.
605 hastanın dahil edildiği çalışma,

**Biochemical recurrence-free survival**




**Clinical recurrence-free survival**



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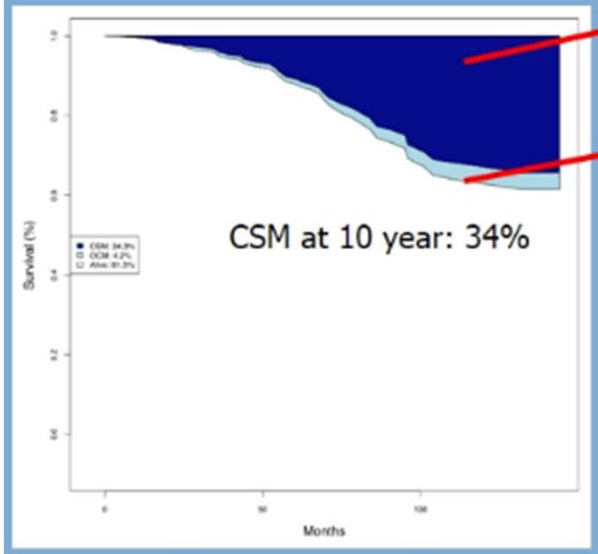
# LONG TERM OUTCOMES OF SALVAGE LND




Cancer-specific mortality

Other-cause mortality

**Competing risk regression to predict CSM**

| Variable | Subhazard Ratio | 95% Confidence Interval | p-value |
|---|---|---|---|
| ISUP grade at RP | | | |
| ≤4 | Reference | - | - |
| ≥5 | 1.67 | 1.00, 2.79 | 0.051 |
| HT administration at PET/CT scan | 2.78 | 1.68, 4.61 | <0.0001 |
| PSA at SLND | 1.00 | 1.00, 1.01 | 0.2 |
| Number of nodes removed at SLND | 1.00 | 0.98, 1.01 | 0.6 |
| Number of positive nodes at SLND | | | |
| ≤2 | Reference | - | - |
| 3+ | 1.81 | 1.07, 3.04 | 0.026 |
| Post-SLND therapy | | | |
| Hormonal therapy | 0.27 | 0.16, 0.45 | <0.0001 |
| Radiotherapy | 0.55 | 0.33, 0.90 | 0.018 |
| Chemotherapy | 1.04 | 0.54, 2.01 | 0.9 |

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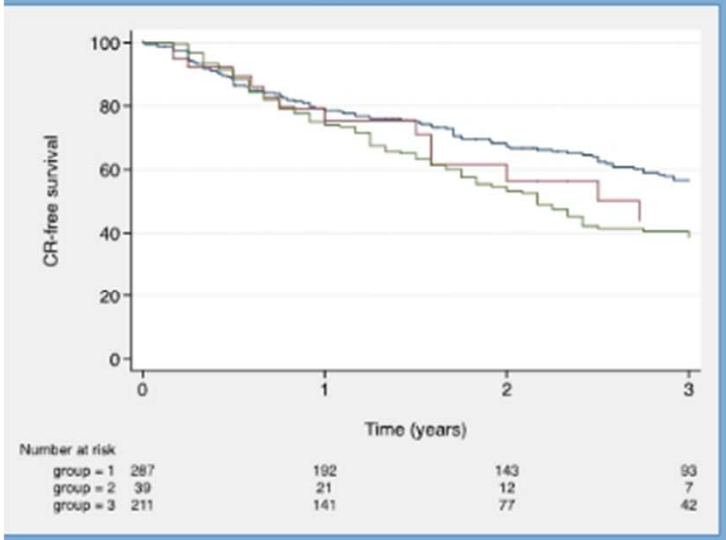
# IMAGING TARGETED TREATMENTS VERSUS EXTENDED SALVAGE LYMPH NODE DISSECTION FOR PATIENTS WITH A SINGLE NODAL RECURRENCE OF PROSTATE CANCER: A COMPARATIVE ANALYSIS FROM A LARGE MULTI-INSTITUTIONAL SERIES

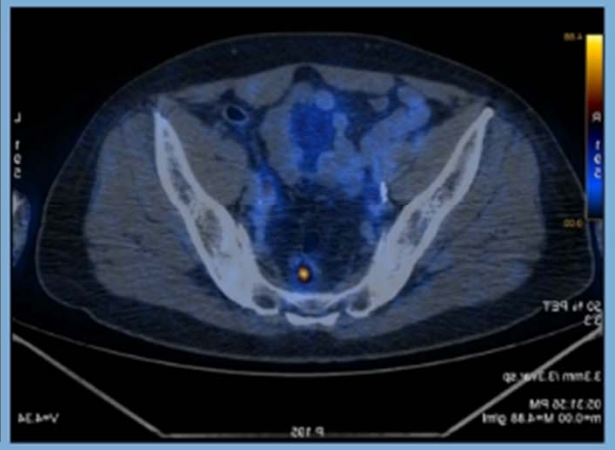
✓ Retrospective analysis of 567 men with single-node recurrence treated with elective resection of the node (n=41), targeted SBRT (n=211) or extended PLND (n=315)




Rekürrenssiz sağkalım oranları

- E-LND: %58
- SBRT: %40
- T-LND: %41

E-LND en iyi yöntem ancak SBRT ile T-LND arasında fark yok.



Results confirmed at MVA

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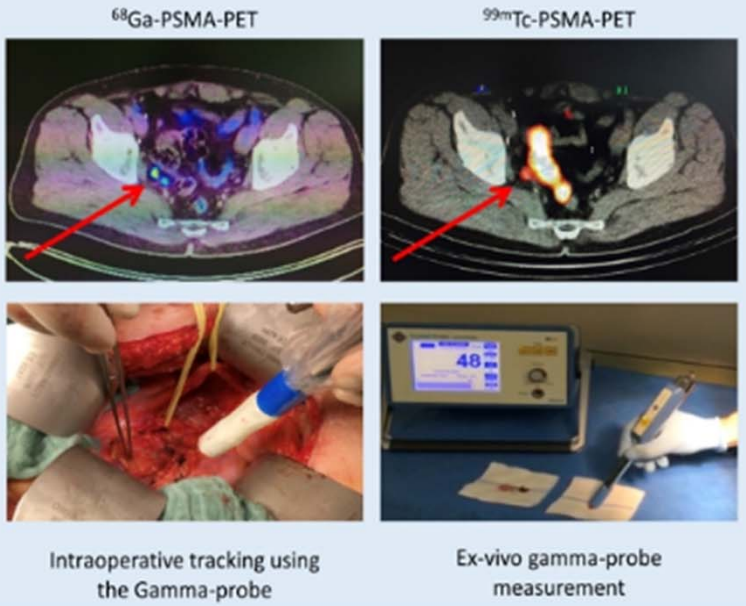
# IMAGING TARGETED TREATMENTS VERSUS EXTENDED SALVAGE LYMPH NODE DISSECTION FOR PATIENTS WITH A SINGLE NODAL RECURRENCE OF PROSTATE CANCER: A COMPARATIVE ANALYSIS FROM A LARGE MULTI-INSTITUTIONAL SERIES




ADT almamış, PSMA-PET yapılan 47 hasta
27 hasta- E-SLND
20 hasta T-SLND

| PSA-decline | RGS (n=20) | CSA (n=27) | *p*-value |
|---|---|---|---|
| Overall | 20 (100%) | 14 (52%) | 0.001 |
| >50% | 16 (80%) | 8 (30%) | <0.01 |
| >90% | 10 (50%) | 2 (7%) | <0.01 |

Radyo-rehberli cerrahiler kısa dönemli PSA düzelmeleri için umut verici, ileri çalışmalar yapılmalı.

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# Testing Radical prostatectomy in men with prostate cancer and oligoMetastases to the bone (TRoMbone): a randomized controlled feasibility trial

Fizibilite çalışması, 50 hasta randomize edilmiş.
Dosetaksel
Dosetaksel + RP

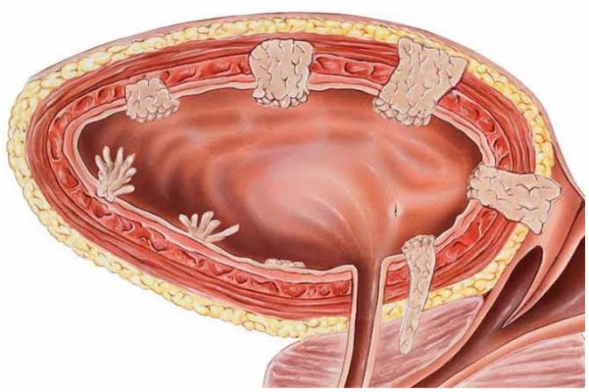
- ✓ No abandoned surgeries
- ✓ Median (IQR) op time 3h (2.8-4.0)
- ✓ Median (IQR) LOS 2d (2-2)
- ✓ Median (IQR) cath duration 14d (12-15d)

Complications: 1/25 blood transfusion (2 units); 1/25 rectal injury (repaired intraop); 1/25 infected lymphocele → sepsis → pericarditis (readmitted to ITU post-discharge)


Daha önce yapılan çalışmalarda sitoredüktif cerrahinin
GU komplikasyonlar
Transfüzyon oranları
Hastanede kalış süresi
Maliyet +%20

Yüksek volümlü merkezlerde kullanılabilir bir tedavi haline gelebilir.

# Mesane Kanseri



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## *FGFR3* mutation and FGFR3 expression & Clinical Outcome in RC Implications for anti-FGFR3 Bladder Cancer Treatment?

1. *FGFR3* mutations are associated with favorable prognosis (N)MIBC
2. FGFR3 over-expression is also found in 40% FGFR3 wild-type MIBC
3. FGFR3 receptor: Actionable Target

FGFR 3 mutasyon ve ekspresyonunun klinikopatolojik parametrelere ve prognoza etkisi, Çok merkezli çalışma

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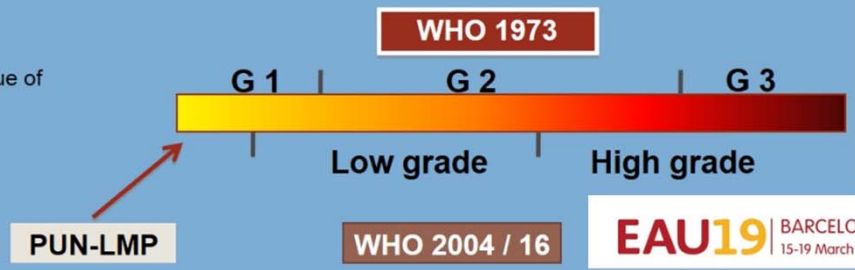
PROGNOSTIC VALUE OF THE WHO 1973 AND 2004/2016 GRADING SYSTEMS IN PRIMARY Ta/T1 NON-MUSCLE INVASIVE UROTHELIAL CARCINOMA OF THE BLADDER - A MULTICENTER EAU NMIBC GUIDELINES PANEL STUDY

## Grade: Important Prognostic Factor in NMIBC

**EAU Guideline:** WHO1973 & WHO2004/16
**AUA Guideline:** Only WHO 2004/16

**Objective:**
Compare Prognostic Value of these Two Classification Systems for Grade

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PROGNOSTIC VALUE OF THE WHO 1973 AND 2004/2016 GRADING SYSTEMS IN PRIMARY Ta/T1 NON-MUSCLE INVASIVE UROTHELIAL CARCINOMA OF THE BLADDER - A MULTICENTER EAU NMIBC GUIDELINES PANEL STUDY

- **Individual patient data for 5049 primary (first diagnosis) Ta/1 NMIBC patients from 17 centers**
- **Univariate and multivariable Cox regression analyses of WHO1973 and WHO2004/16 stratified by center were performed for time to recurrence, progression (primary endpoint), cystectomy and survival taking into account treatment, stage, concomitant CIS, size, multiplicity, gender and age**
- Mean age was 67 years, 3292 (65%) patients were Ta
- WHO1973: 1112 (22%) G1 2537 (50%) G2 1400 (28%) G3 tumors
- WHO2004/16: 76 (1%) LMP 2467 (49%) LG 2506 (50%) HG tumors
- Median follow-up 3.9 years: 2187 (43%) recurred, 376 (7.5%) progressed (>T1), 301 (6%) Cystectomy; 856 died (17%), 149 (3%) of bladder cancer
- **No Grading system predicted recurrence**

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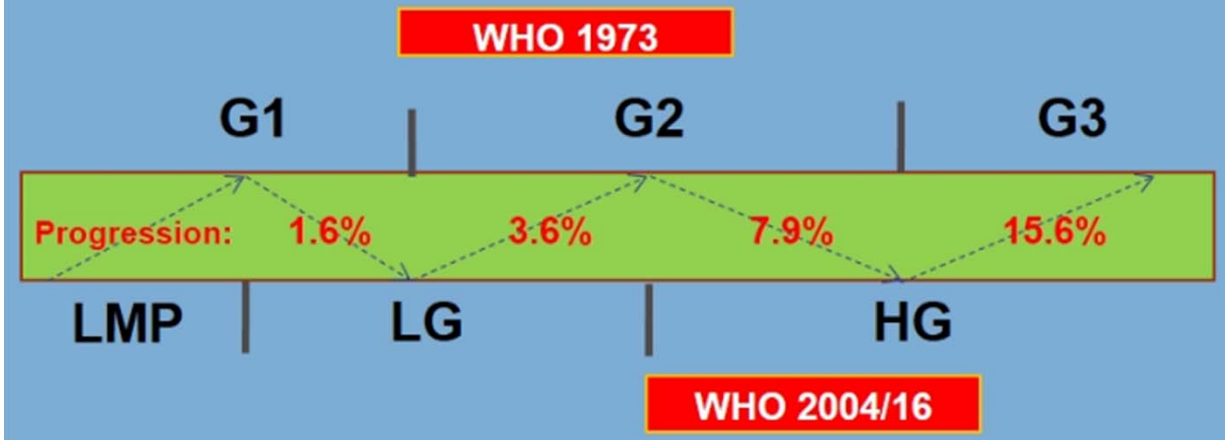
# Prognostic Value of the WHO 1973 and 2004/2016 Grading Systems in Primary Ta/T1 Non-Muscle Invasive Urothelial Carcinoma of the Bladder - A Multicenter EAU NMIBC Guidelines Panel Study

1. WHO1973 & 2004/16 both Predict Progression, DSS and OS, but not Recurrence
2. Greatest Prognostic Value: Combination of WHO1973 and 2004/16
3. EAU NMIBC Guidelines Recommendation to use both WHO Systems Remains Correct



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Mesane kanseri Kas invaziv N1M0 hastalar

***Comparison of different treatment modalities outcomes in clinically node-positive bladder cancer; analysis of a population-based cancer registry.***

Retrospektif

- Retrospective study (N= 749)
- Comparison of different treatment modalities
  - cystectomy + lymphadenectomy + chemo (N= 111)
  - cystectomy + chemo (N=121)
  - chemotherapy alone (N= 195)
  - cystectomy + lymphadenectomy (N=94)
  - cystectomy alone (N=140)
- Methological limits

**Combination radical surgery + chemotherapy + lymphadenectomy offers the best overall survival! #eauguidelines**

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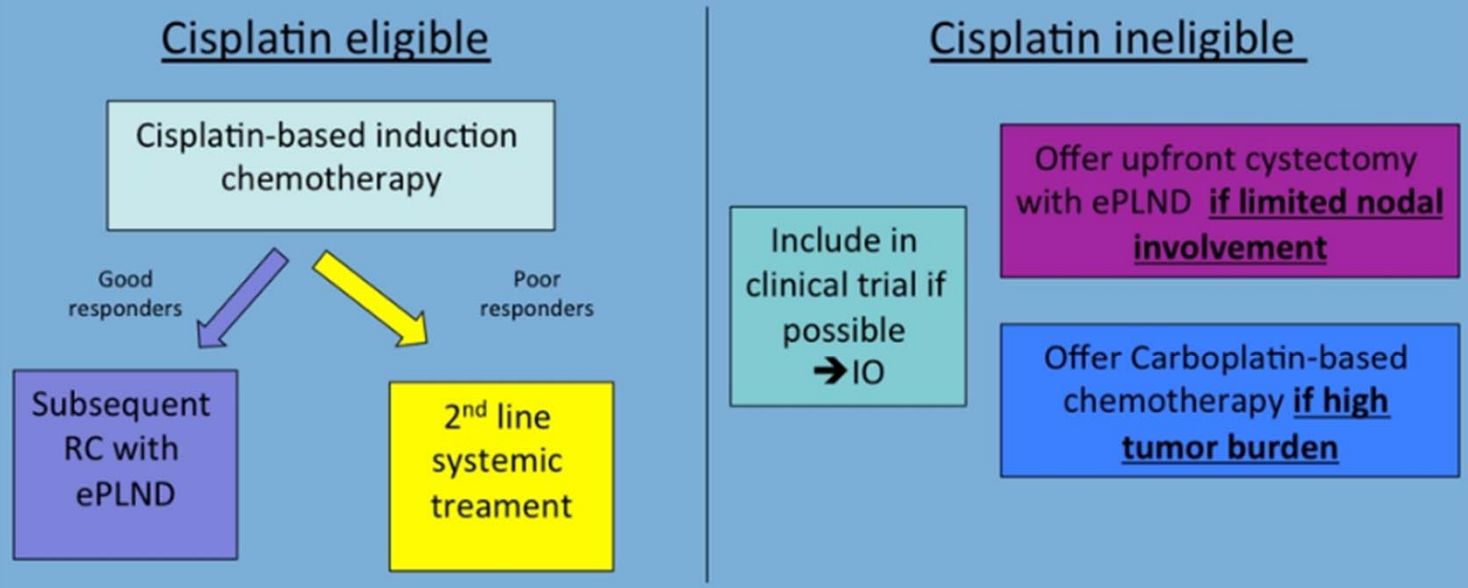
# Mesane kanseri Kas invaziv N1M0 hastalar

**Debate during thematic session 03: « limited pelvic lymph node involvment in otherwise localised disease »**

**Consensus obtained bases on the following flow chart:**




**Primary endpoint:**
- Safety

**Secondary endpoints:**
- Overall survival
- Progression-free survival
- Overall response rate
- Disease control rate
- Duration of response

# SAUL Study - Atezolizumab

**SAUL enrolled a broader patient population with pretreated locally advanced/metastatic urinary tract carcinoma, including patients with**

- Non-measurable disease
- ECOG PS 0–**2**
- Progression on prior non-platinum treatment
- Creatinine clearance ≥15 mL/min
- Stable CNS metastases
- Steroid treatment ongoing at baseline[a]
- Autoimmune disease
- HIV-positive status
- Requirement for renal dialysis

**Between 30 Nov 2016 and 16 March 2018, 1004 patients were enrolled (997 treated) from sites in 32 countries worldwide**

Güvenlik çalışması
1000 hasta
32 ülke
otoimmün hastalık
KBY
HIV
Diyaliz
ECOG 0-2

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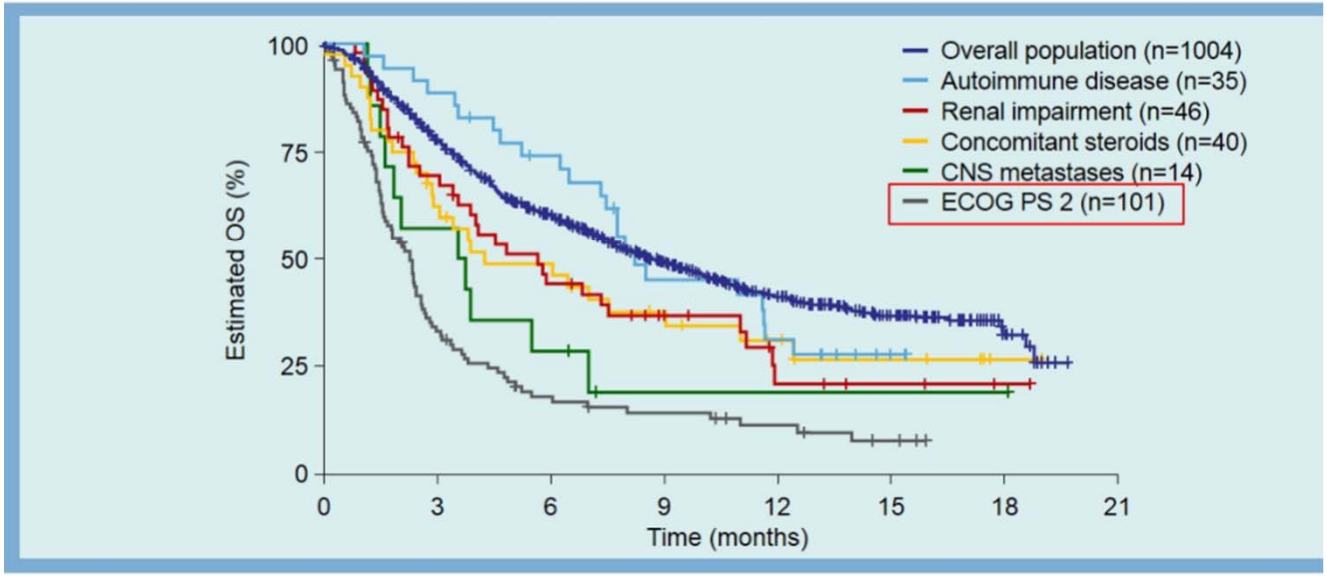
## Overall survival in subgroups of special interest




Toksisite yok.

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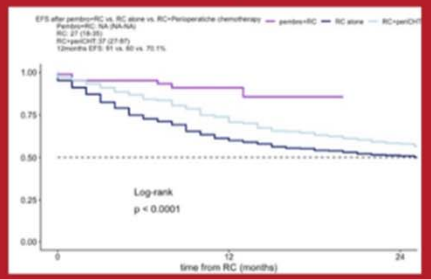
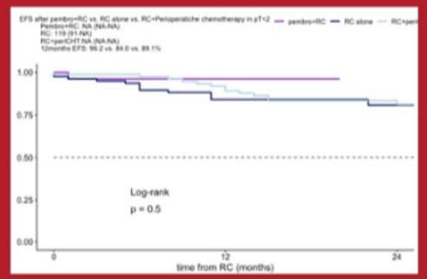
## Propensity score-matched analysis: *PURE-01 (N=84) vs RC ± perioperative CT (N=601)*

Best Poster

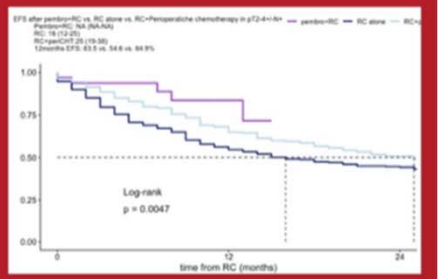
EFS – Overall population




EFS – (y)pT<2




EFS – (y)pT2-4 ± N+




**Overall 12-month RFS:**

| | 12-month RFS | | |
|---|---|---|---|
| **pT stages** | Pembro + RC (n) | RC alone (n) | RC + peri CT (n) |
| **pT<2 (211)** | 98.1% (52) | 88.6% (79) | 91.8% (80) |
| **pT2-4N0-X (412)** | 100% (15) | 66.3% (267) | 74.5% (130) |
| **pN+ (225)** | 76.7% (17) | 38.7% (93) | 60.5% (115) |



Bandini M, et al. Poster Session 80, March 18. Abstract 1122

European Association of Urology

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**Can we predict response and survival after neoadjuvant chemotherapy?**

| Biomarker | N | Translational relevance | Reference |
|---|---|---|---|
| ERCC2 mutation | 50 | Association with pathologic response | *Van Allen EM et al. Cancer Discov 2014* |
| ERCC2 mutation | 48+54 | Association with improved OS in 2 independent cohorts of cisplatin-treated MIBC patients | *Liu D et al. JAMA Oncol 2016*<br>*Plimack ER et al. Eur Urol 2015*<br>*Plimack ER et al. ASCO 2014* |
| ATM/RB1/FANCC mutations | 34 | Association with improved pT<2 response and OS | *Plimack ER et al. Eur Urol 2015* |
| ATM/RB1/FANCC mutations | 25 | Association with improved pT<2 response | *Anari F et al. Eur Urol Oncol 2018* |
| ERBB2 mutations | 71 | Association with pT0 response | *Groenendijk FH et al. Eur Urol 2015* |
| DNA damage response (DDR) gene alterations | 46 | Association with pT<2 response and RFS with dose-dense GC | *Iyer G et al. J Clin Oncol 2018* |
| Single-sample genomic subtyping classifier | 343 | Basal tumors benefited the most from neoadjuvant chemotherapy administration | *Seiler R et al. Eur Urol 2017* |

**Can we predict response and survival after neoadjuvant IO?**

- PD-L1
- TMB/gLOH/MSI
- GEP/IFN-γ signature
- CD8 infiltration
- EMT signature
- Circulating markers: MDSCs, cytokines, mutations/ctDNA
- Immune components of the TME: CD8/Tregs/ TGFβ/MDSCs/TAMs, others
- Others: subtyping, mutations, etc.

**İleride hangi hastaların neo-adjuvan tedaviden yarar göreceğini belirlemek için markerlar belirlememiz gerekecek.**

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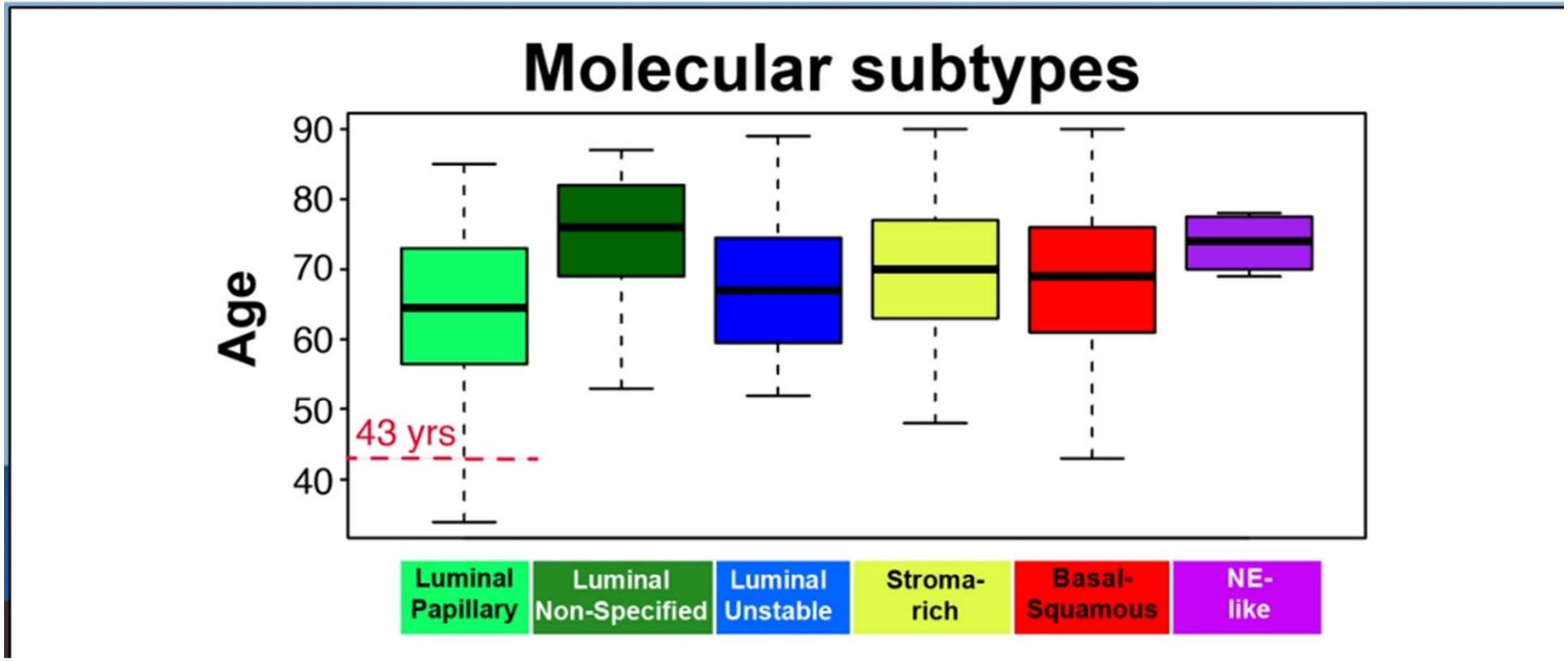
# Consensus on classification



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## Impact of the number of radical cystectomies per hospital on 90-day mortality in Spain

Mortality after RC in literature: 2.3 à 7.9%

Sistektomi yüksek volümlü merkezlerde yapılmalı. ( >38/Yıl)

Spanish register study 2011-2015

12154 RC/ 196 hospitals

- Majority of hospitals do less than 10 RC/ year
- Only 5 are doing more than 38/year

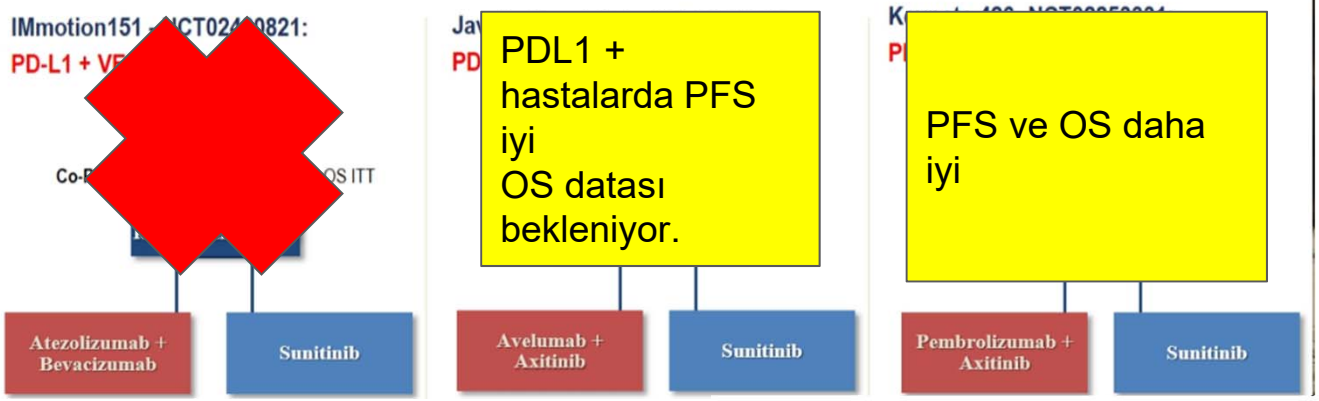
Mortality at 30-, 60- et 90-days= 2.9%, 5.1% and 6.5%

Lower rate= 3.3% at 90 days in high volume (i.e; > 38 /year)

Every 10 RC/year → 20% of decrease in mortality at 90 days ($p<0.001$)

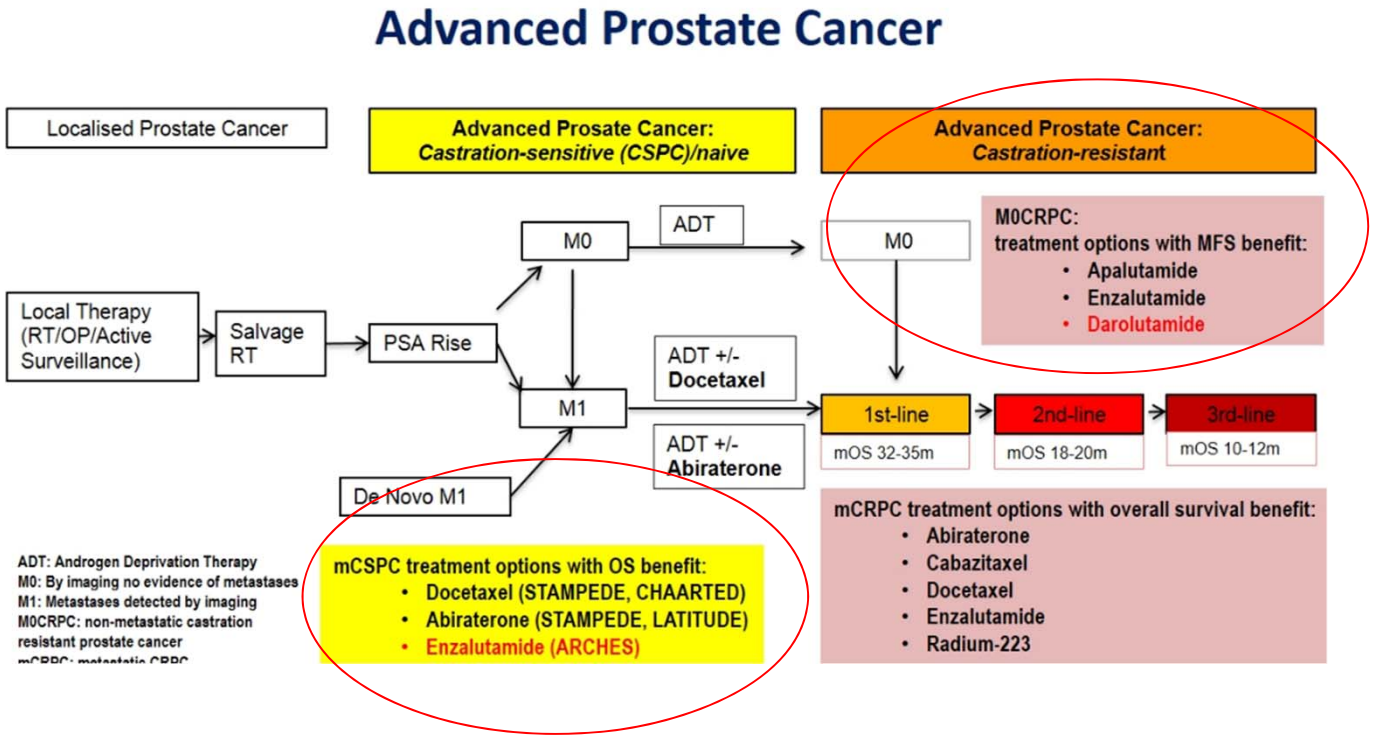
# Sistemik Tedaviler

## Metastatic clear cell RCC: COMBINATION TRIALS




## ccRCC :The current and future treatment options

| First-Line | Second-Line | Third-Line |
|---|---|---|
| **Favourable Risk:** **Sunitinib / Pazopanib** | Axitinib<br>Cabozantinib<br>Nivolumab<br>Lenvatinib/Everolimus<br>Everolimus | Axitinib<br>Cabozantinib<br>Nivolumab<br>Lenvatinib/Everolimus<br>Everolimus |
| About to arrive:<br>Axitinib/Pembro<br>Axitinib/Avelumab<br>Biomarker PD-L1? | | |
| **Intermediate / Poor Risk** **Nivolumab/Ipilimumab** (selected pts: Cabozantinib) | Sunitinib<br>Pazopanib<br>Axitinib<br>Cabozantinib<br>Lenvatinib/Everolimus<br>Everolimus | Sunitinib<br>Pazopanib<br>Axitinib<br>Cabozantinib<br>Lenvatinib/Everolimus<br>Everolimus |




Kastrasyon naiv metastatik prostat kanseri

Enzalutamid(ARCHES)

Kastrasyon dirençli non-metastatik prostat kanseri

Darolutamid(ARAMIS)

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## ARCHES study design

**Key eligibility criteria**

- mHSPC (confirmed by bone scan, CT or MRI), histologically confirmed adenocarcinoma
- ECOG PS score of 0 or 1
- Current ADT duration ≤3 months unless prior docetaxel, then ≤6 months

**Stratification factors**

- Volume of disease (low vs high*)
- Prior docetaxel therapy for mHSPC (none, 1–5 or 6 cycles)

n=1150

R 1 : 1

Enzalutamide 160 mg/day + ADT

Pl

**Key discontinuation criteria**

Radiographic progression, unacceptable toxicity or initiation of an investigational agent or new therapy for prostate cancer

21 March 2016

14 October 2018

**Primary endpoint**

- rPFS: time from randomisation to first objective evidence of
  cause within 24 weeks of treatment discontinuation, whichev
  - Radiographic disease progression was defined by RECIST, ver
    lesions on bone scan compared to baseline (at week 13) or vers
    lesions observed at week 13 required confirmation of ≥2 additio

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*Defined as metastases involving the viscera or, in the a
bony structure beyond the vertebral column and pelvic b
CT=computed tomography; ECOG PS=Eastern Coopera
MRI=magnetic resonance imaging; OS=overall survival,

ENZA+ADT >ADT+Placebo

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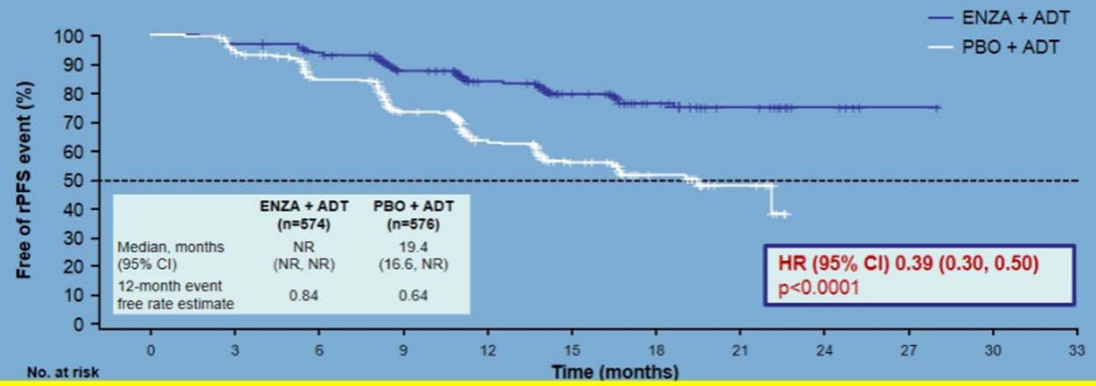
## ARCHES: Overall rPFS




The combination of ADT and Enzalutamide has acceptable toxicity in the medium term

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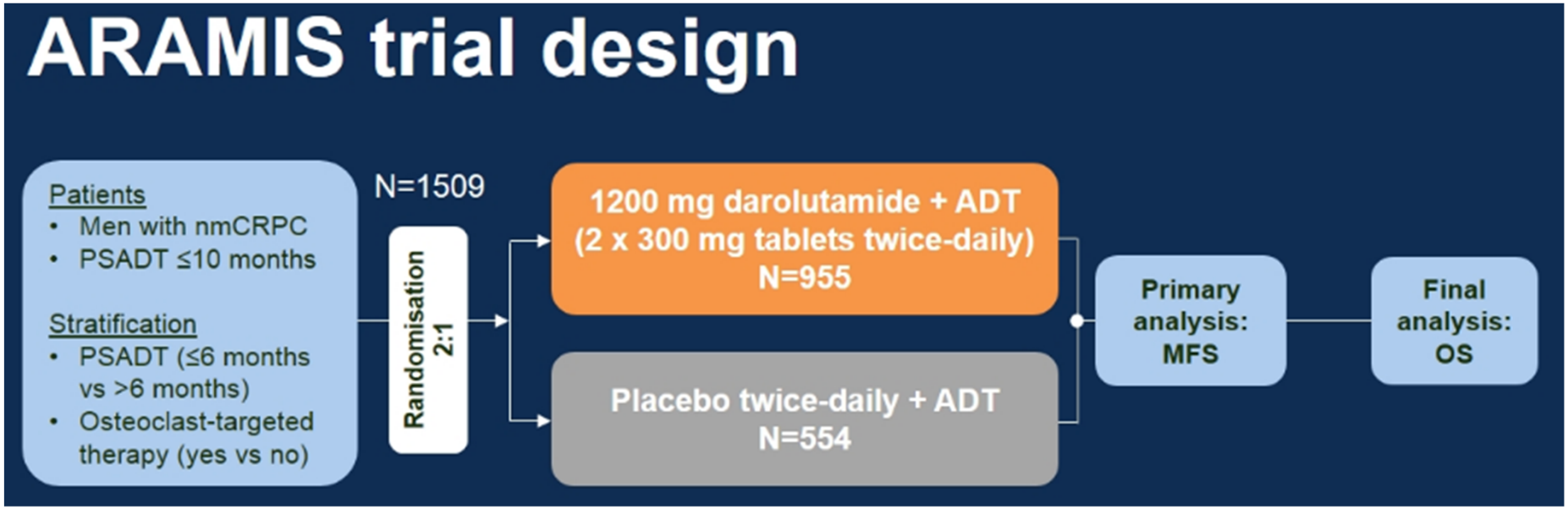
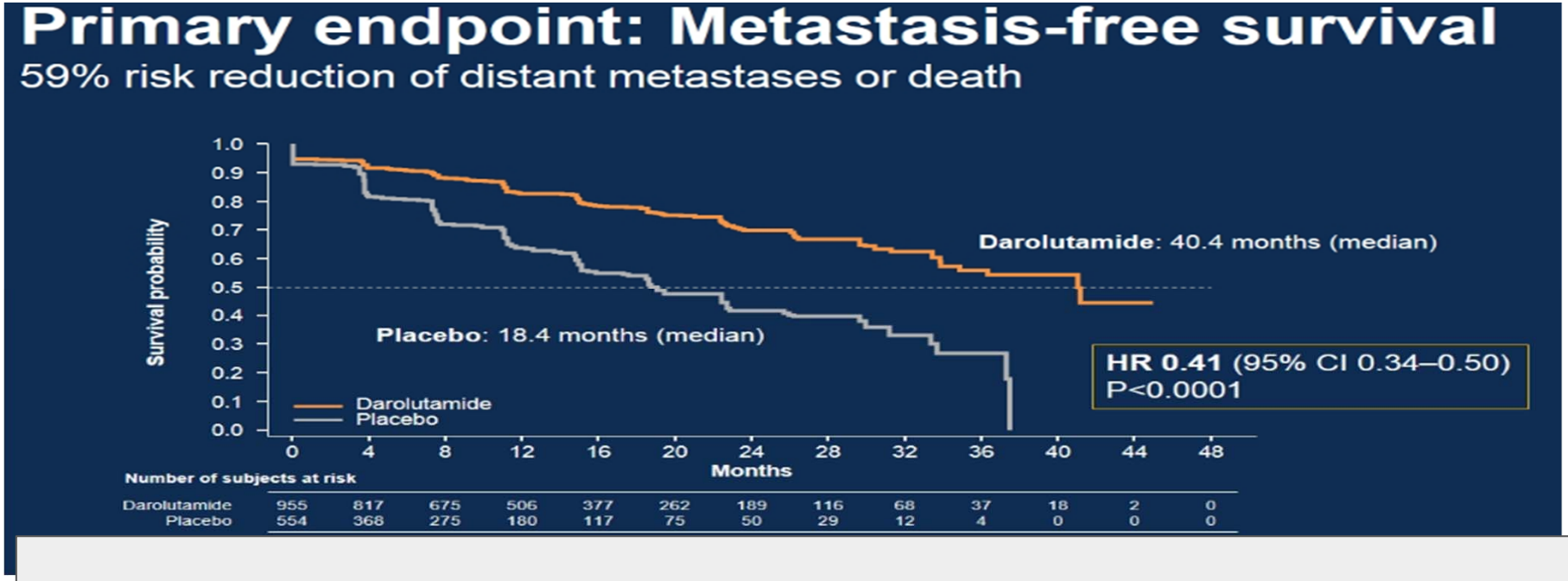
Presented by discussant N Clarke

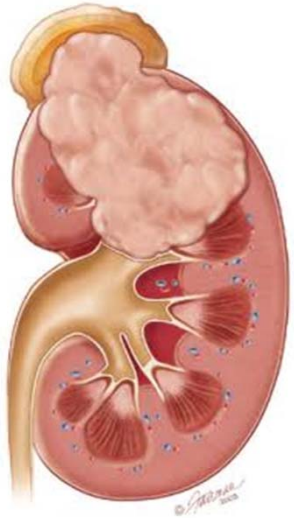
European Association of Urology


ARAMIS trial design
Patients
• Men with nmCRPC
• PSADT ≤10 months
Stratification
• PSADT (≤6 months vs >6 months)
• Osteoclast-targeted therapy (yes vs no)
N=1509
Randomisation 2:1
1200 mg darolutamide + ADT (2 x 300 mg tablets twice-daily) N=955
Placebo twice-daily + ADT N=554
Primary analysis: MFS
Final analysis: OS




- Non-metastatik kastrasyon dirençli prostat kanseri hastalarında
- Darolutamid vs. Placebo
- Androjen reseptör inhibitörü
- PSA düşüşü sağlıyor
- PSA progresyonunu engelliyor
- Metastazsız sağkalımı uzatıyor
- Total sağkalım üstüne etkisi belirsiz
- ARASENS çalışması bekleniyor

# Böbrek Tümörleri



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# Renal autotransplantation for RCC

**The Oxford Experience**

- 36 patients, 2005-2018
- mainly solitary kidneys
- Tumor size 6.2 cm, 34/36 highly complex

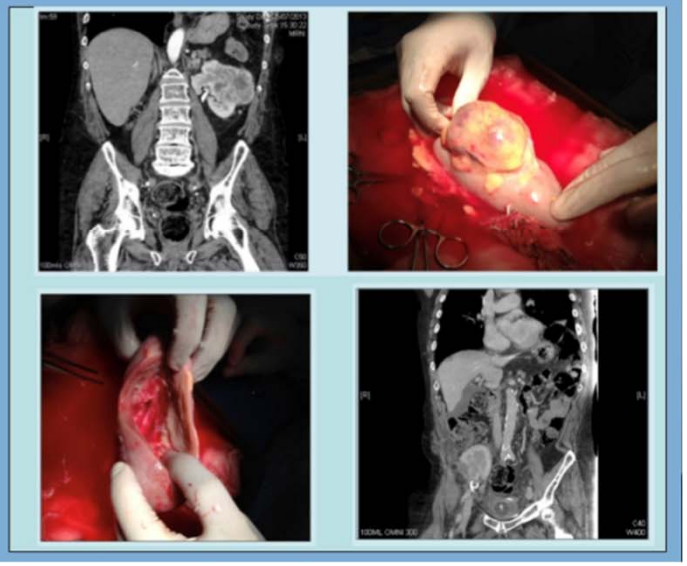
**Outcomes:**

- PSM 3/36 (5.6 %)
- Clavien III-V complications 20/36 (56 %)
- Mortality 2/36 (5.6 %)

**60-months Follow-up:**

- CSS 96 %
- Recurrence-free 79 %
- Dialysis-free 83 %

➢ Chance for renal preservation without compromising cancer control but complex and potentially hazardous



# Indications and oncological outcomes of the use of neoadjuvant targeted therapy in patients with localized kidney cancer

Voylenko O., Stakhovskyi O., Kononenko O., Pikul M., Semko S., Vitruk Y, Stakhovsky E.
Department of Plastic and Reconstructive Oncological Urology, National Cancer Institute, Kyiv, Ukraine

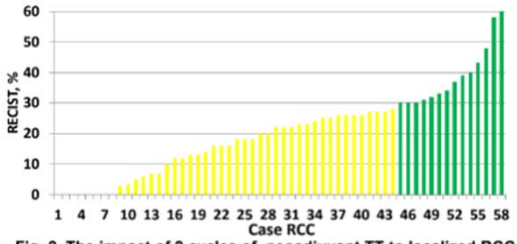



Fig. 2. The impact of 2 cycles of neoadjuvant TT to localized RCC (% of regression)

Fig. 3. Dependence of tumor size RCC and % of regression

The effects of TT prompted to proceed to partial nephrectomy in 53 cases (91,4%) over only 22 (33,3%) in only surgery group ($x^2 = 42,1$; $p < 0,001$) (**Fig.4**).

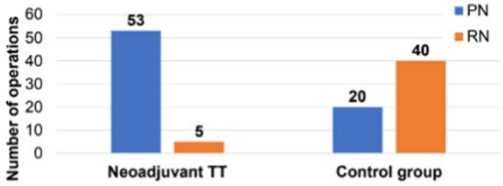



Fig. 4. Number of operations in comparison groups

Prospektif Randomize
58 hasta pazopanib ( 2 kür)
60 hasta sadece cerrahi
Temel parametreler benzer

Neoadjuvan tedavi alan grupta
- Parsiyel nefrektomi oranları daha fazla
- 20.5 mm ortalama tümör boyutu azalmış
- %91 pazopanib sonrası parsiyel
- %33 tedavisiz parsiyel nefrektomi oranları

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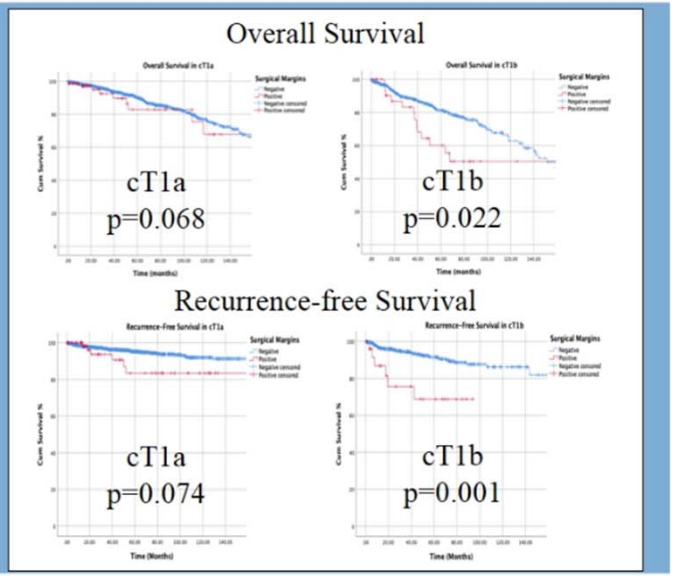
## Impact of PSM in cT1a/cT1b Tumors

**Retrospective multicenter analysis of 2737 patients undergoing partial nephrectomy**

- **cT1a: 1842 cT1b: 774**
- **PSM: 113 (4.3 %)**
- **Median Follow-up: 44.4 months**
- **Uni- and multivariate analysis**
- **PSM (and cT1b vs. cT1a) independent predictor of recurrence-free survival (HR 2.761)**

➢ **Patients with cT1b R1 tumors are at increased risk for recurrence and mortality => closer follow-up**




tamamlayıcı bir tedavi önerilmiyor.

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## Outcome after PN vs. RN in the young+healthy

**National Cancer Database analysis, 2004-2007**

**Inclusion criteria:**

- **Patients <50 years of age, cT1 RCC**

**Demographics and Outcomes:**

- **Median age 44 years**
- **2454 radical nephrectomies**
- **555 partial nephrectomies (18.4 %)**
- **Median Follow-up: 109 months**
- **No difference in long-term OS**

➢ **No need to take an oncological risk in the young and healthy patient with highly complex tumors**