Managing Prostate Cancer After Initital Treatment Fails: Are There Good Next Steps?

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Options After Failed First Treatment

- Good options to consider after Surgery
- Good options to consider after Radiation
- Good options to consider if the disease spreads to bone

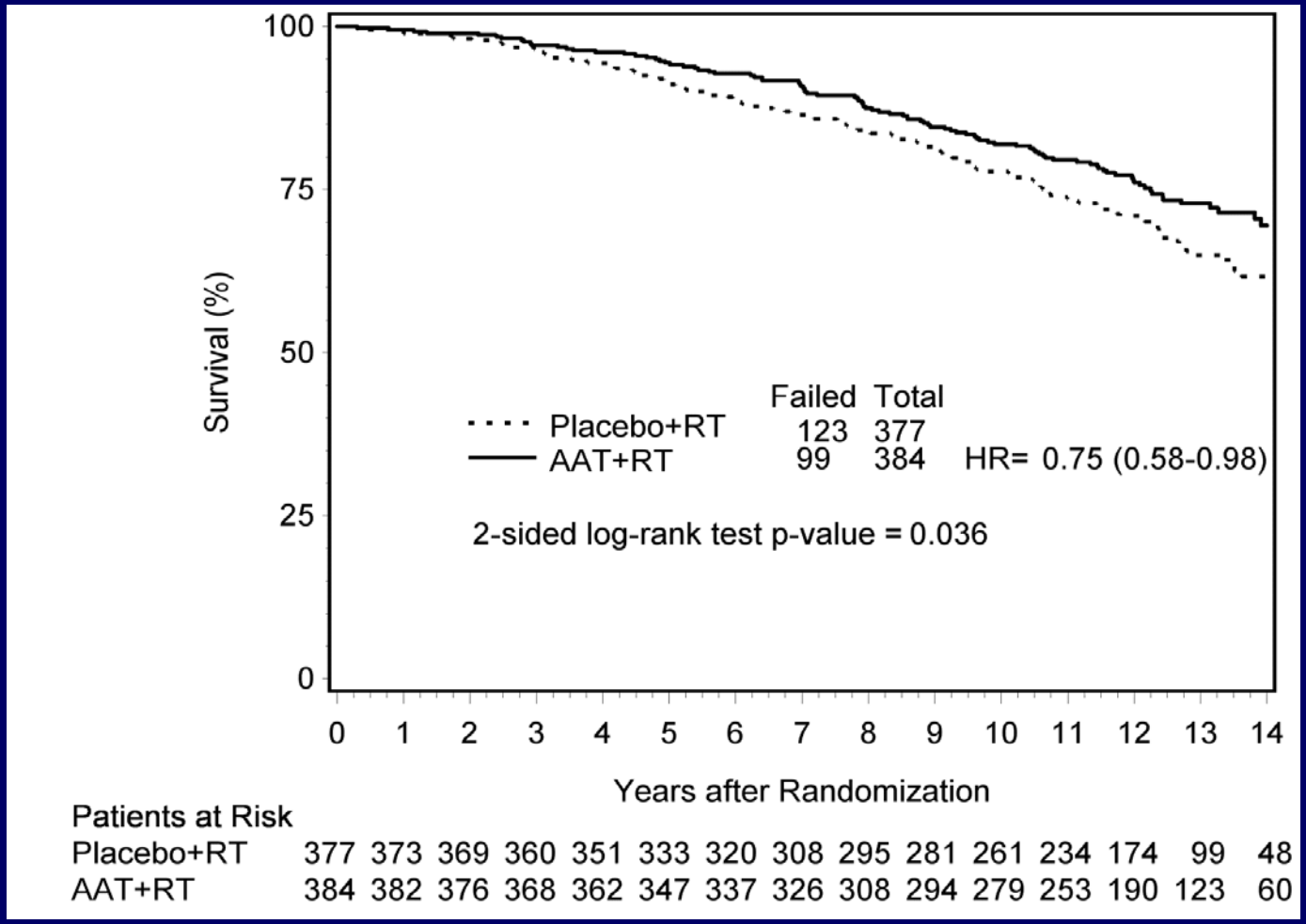
Treatment Failure after Surgery

- PSA rises from undetectable to a detectable levels
- Generally we watch over a period of several months to make sure this is a real rise.
- Once documented rising PSA level, routine tests done such as MRI and bone scan to confirm no disease has spread

Treatment Options after Failed Surgery

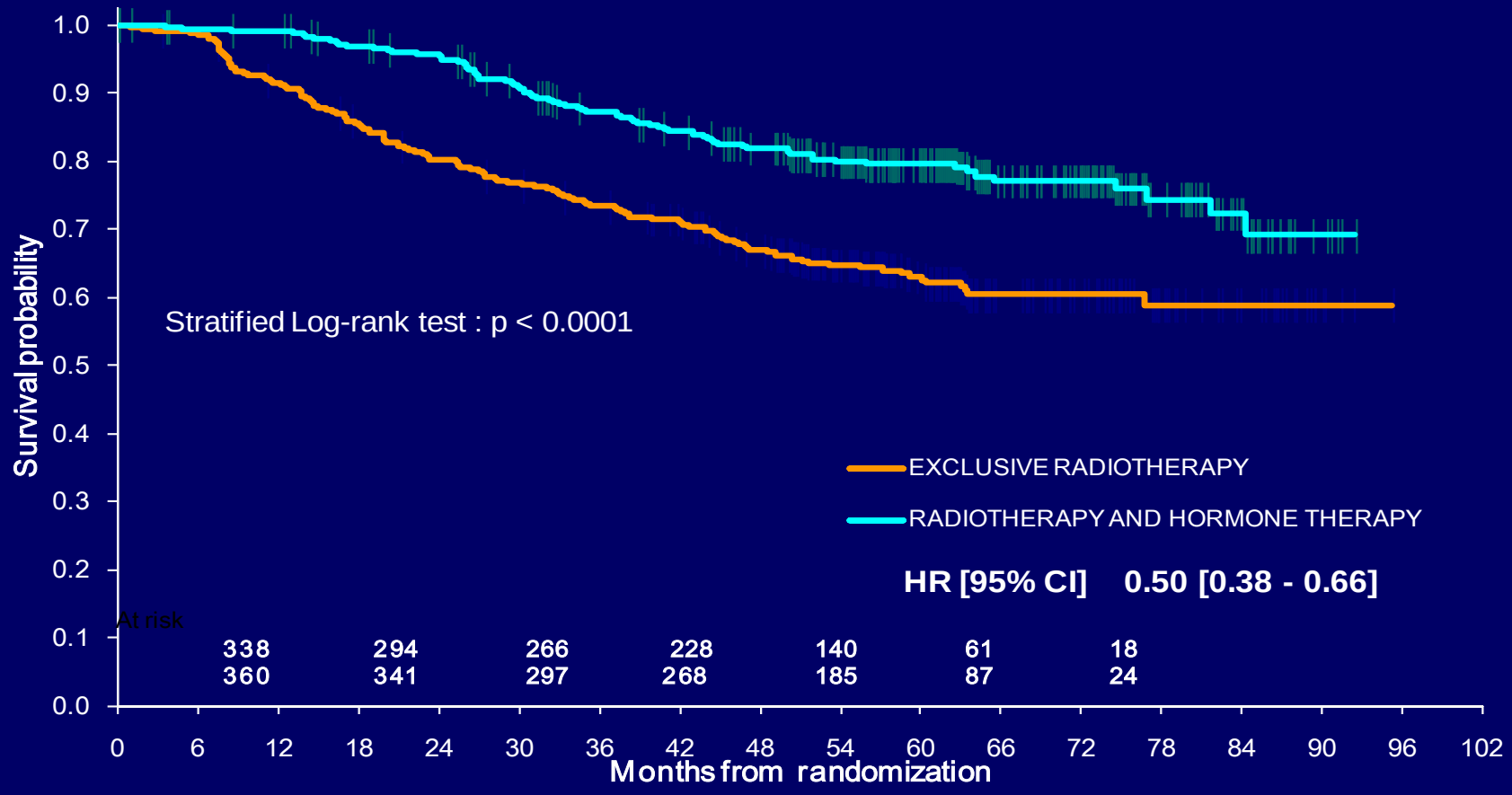
- If studies such as MRI and bone scan show no spread then radiation treatments to the “prostate bed” and sometimes the lymph nodes are given.
- This treatment is given daily Monday – Friday for 8 weeks
- Recent studies show that adding hormones to the radiation treatments is associated with higher success rates

After Failed Surgery
Cure Rates RTOG 9601
Role of Adding Hormones to the Radiation

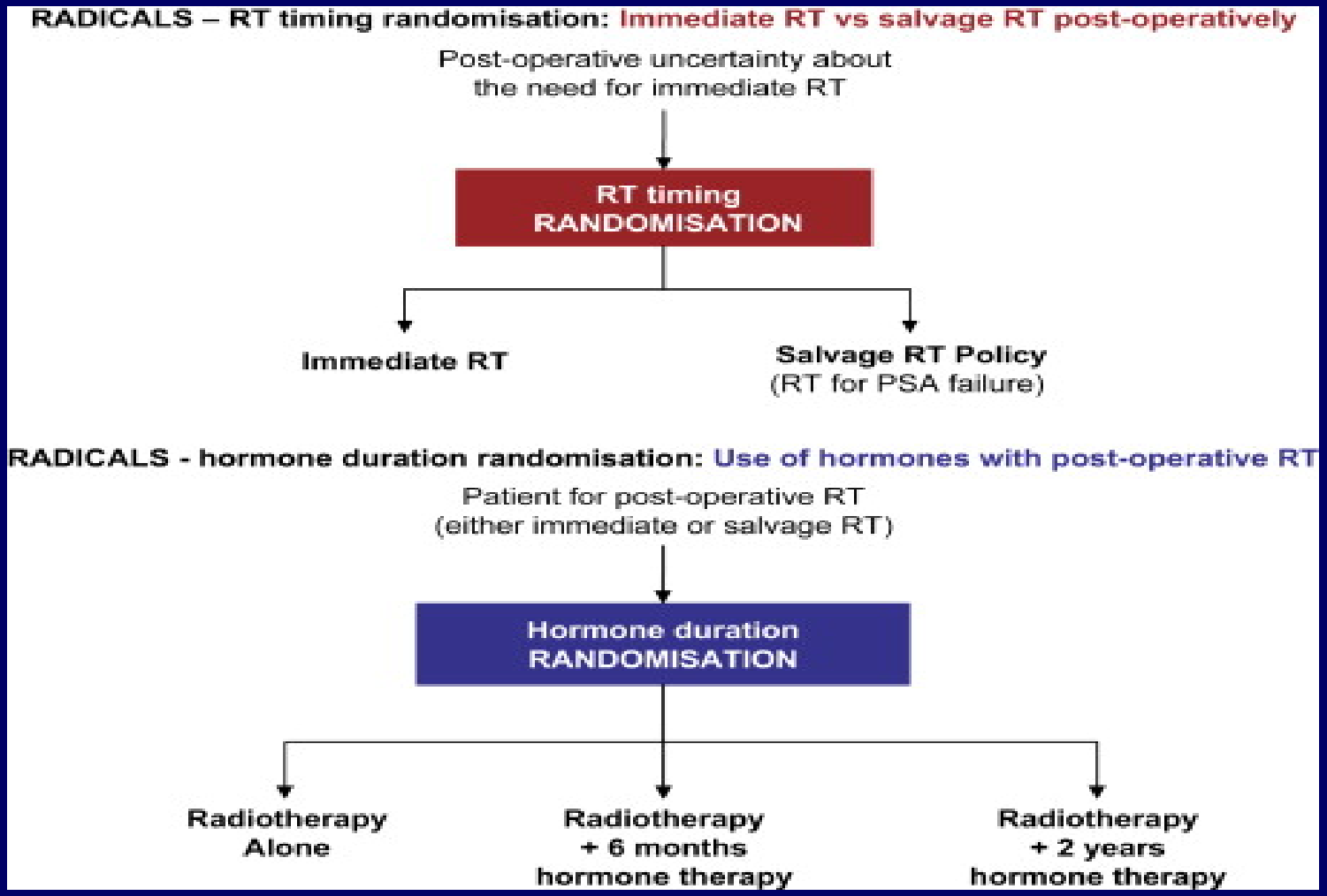


OS at 10 yrs:
82% vs 78%

Improved Progression Free Survival Using Hormones with Radiotherapy GETUG-AFU 16



RADICALS Trial
(Radiotherapy and Androgen Deprivation in Combination with Local Surgery)



When Primary Radiation is Not Effective- Next Steps

- Recurrence is suspected if the PSA goes up
- Scans are done to confirm there is no disease elsewhere
- Biopsy of the Prostate to confirm if the cancer is still present in the gland

Post-treatment biopsies

- MRI-guided biopsies when feasible

- Difficult to interpret
  - Severe tissue changes can be seen which looks like cancer but is not viable disease
  - May be confounded by hormonal changes in the tissue

Does earlier treatment of locally recurrent cancer make a difference?

- Beyer et al (Urol 1999) and Henriquez et al (Radiat Oncol 2014)
  - Improved 5y DFS with presalvage PSA <10ng/mL
- Burri et al (IJORBP 2010):
  - improved 10y PSA RFS with presalvage PSA <6ng/mL
- Grado et al (Brachy 2014):
  - Early treatment (≤5y) after failure vs delayed associated with better biochemical control

Good Options With Recurrence After Radiation

- Salvage surgery with 60% success
- Salvage radiation often with internal radiation therapy known as brachytherapy- success rates of 70% with much less incontinence than surgery
- Hormonal therapy

Evidence Review

THE LANCET

Radiotherapy to the primary tumour for newly diagnosed, metastatic prostate cancer (STAMPEDE): a randomised controlled phase 3 trial

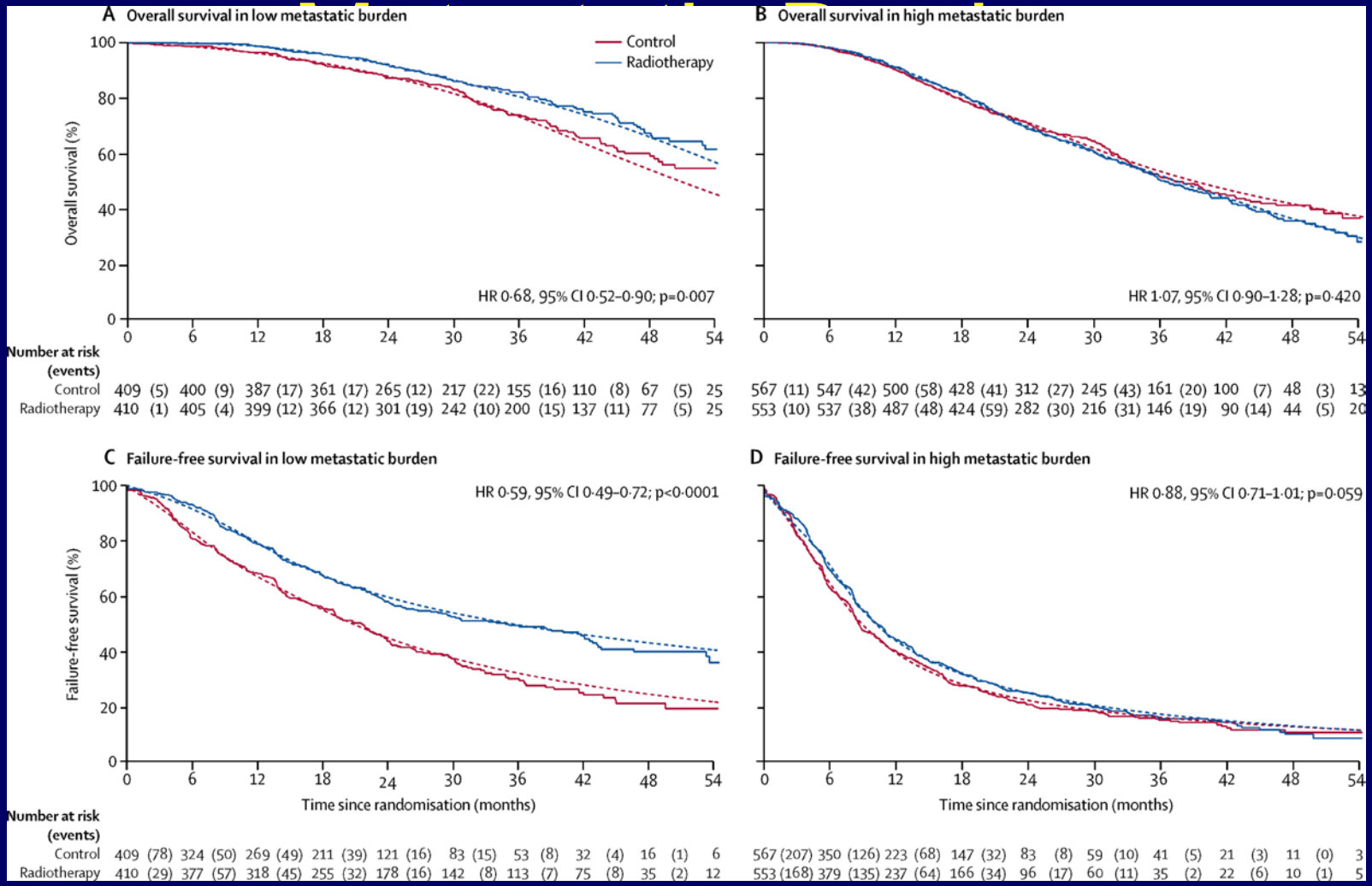
Christopher C Parker, Nicholas D James, Christopher D Brawley, Noel W Clarke, Alex P Hoyle, Adnan Ali, Alastair W S Ritchie, Gerhardt Attard, Simon Chowdhury, William Cross, David P Dearnaley, Silke Gillessen, Clare Gilson, Robert J Jones, Ruth E Langley, Zafar I Malik, Malcolm D Mason, David Matheson, Robin Millman, J Martin Russell, George N Thalmann, Claire L Amos, Roberto Alonzi, Amit Bahl, Alison Birtle, Omar Din, Hassan Douis, Chinnamani Eswar, Joanna Gale, Melissa R Gannon, Sai Jonnada, Sara Khaksar, Jason F Lester, Joe M O'Sullivan, Omi A Parikh, Ian D Pedley, Delia M Pudney, Denise J Sheehan, Narayanan Nair Srihari, Anna T H Tran, Mahesh K B Parmar, Matthew R Sydes*, on behalf of the Systemic Therapy for Advanced or Metastatic Prostate cancer: Evaluation of Drug Efficacy (STAMPEDE) investigators†*

Lancet 2018.
392:2353-66.

Trial Design

- **Hypothesis**: RT to the prostate would improve cure in men with metastatic prostate cancer, and that the benefit would be greatest in patients with a low metastatic burden

Predefined Subset –



Improved OS in patients with low metastatic burden

What Does the Stampede Study Teach Us?

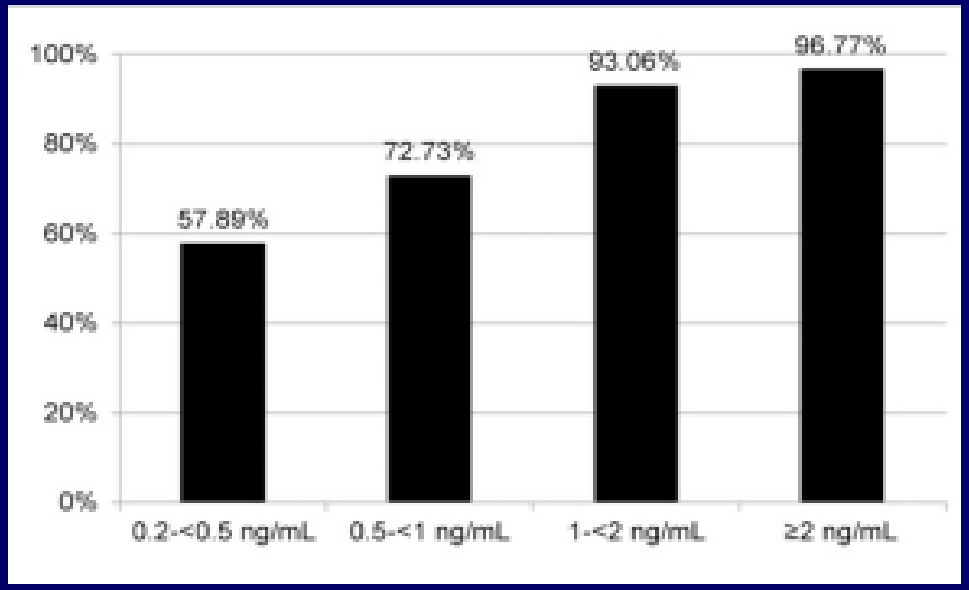
- In patients with low levels of tumor spread to other areas, treating with hormones + adding radiation to the prostate area can increase the cure rates in the long run

Oligometastatic Disease

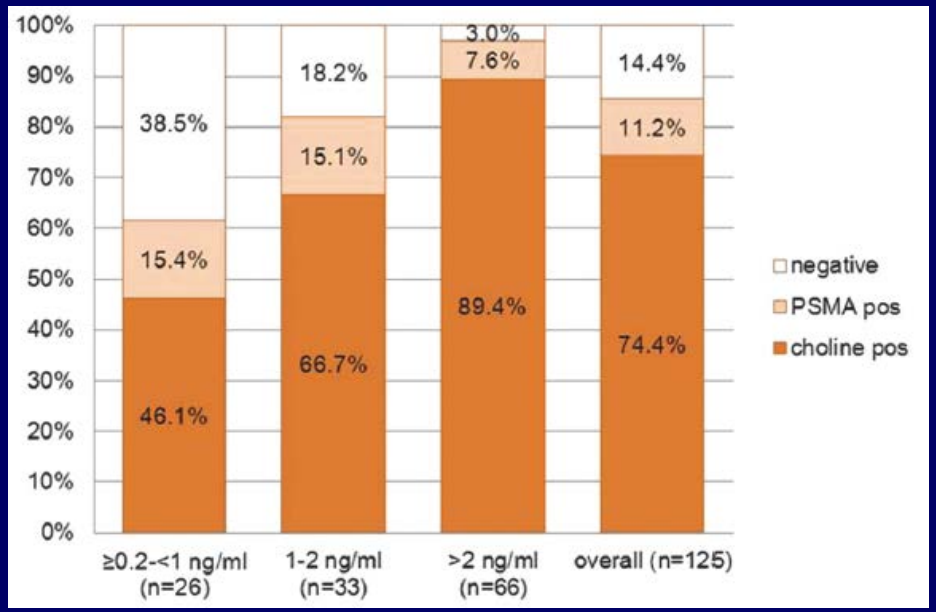
- This disease state is becoming more prevalent due to earlier detection novel imaging such a F18- PET-CT scans and ^{68}Ga-PSMA-11 PET/CT.
- **In particular for patients treated with radical therapy who develop biochemical relapse, imaging prior to salvage or after failed salvage is detecting early metastatic disease.**

PSMA disease detection

PSA level, n=248
BCR after RRP



N=139
F18 Choline pts, serially sequenced with Ga68 PSMA imaging and Choline



Eiber et al JNM (2015)
Afshar-Oromieh et al EJNMMI (2017)
Bluemel Clin Nuc Med 2016

Courtesy of Michael J. Morris, MD

Taking Care of Treatment Failures

- Improved Imaging to help radiation target the areas of disease
- Stereotactic Radiosurgery or SBRT to deliver very high doses to wipe out selected areas of spread which is shown to be effective
- Future research working on targeting sites of spread with radiation that could “ seek out” areas where the PSA shows up and selectively kill those cell
- Use of more targeted therapies taking into account the mutation status noted on gene profiles
- Immunotherapy approaches
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