IX Congresso Internacional de Uro-Oncologia

IV SIMPÓSIO MULTIPROFISSIONAL DE URO-ONCOLOGIA

1 a 3 de Março de 2018

SHERATON SÃO PAULO WTC HOTEL

O teste *Decipher* deve ser usado como exame padrão para prognosticar o câncer de próstata no momento do diagnóstico

Marcelo Langer Wroclawski

IX Congresso Internacional de Uro-Oncologia
1 a 3 de Março de 2018

National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2018
Prostate Cancer

RISK STRATIFICATION AND STAGING WORKUP

Risk group	Clinical/pathologic features	Imaging[i,j]	Molecular testing of tumor
Very low[g]	• T1c AND • Gleason score ≤6/grade group 1 AND • PSA <10 ng/mL AND • Fewer than 3 prostate biopsy fragments/cores positive, ≤50% cancer in each fragment/core[h] AND • PSA density <0.15 ng/mL/g	Not indicated	Not indicated
Low[g]	• T1-T2a AND • Gleason score ≤6/grade group 1 AND • PSA <10 ng/mL	Not indicated	Consider if life expectancy ≥10y[l]
Favorable intermediate[g]	• T2b-T2c OR • Gleason score 3+4=7/grade group 2 OR • PSA 10–20 ng/mL AND • Percentage of positive biopsy cores <50%	• Bone imaging[k]: not recommended for staging • Pelvic ± abdominal imaging: recommended if nomogram predicts >10% probability of pelvic lymph node involvement	Consider if life expectancy ≥10y[l]
Unfavorable intermediate[g]	• T2b-T2c OR • Gleason score 3+4=7/grade group 2 or Gleason score 4+3=7/grade group 3 OR • PSA 10–20 ng/mL	• Bone imaging[k]: recommended if T2 and PSA >10 ng/mL • Pelvic ± abdominal imaging: recommended if nomogram predicts >10% probability of pelvic lymph node involvement	Not routinely recommended
High	• T3a OR • Gleason score 8/grade group 4 or Gleason score 4+5=9/grade group 5 OR • PSA >20 ng/mL	• Bone imaging[k]: recommended • Pelvic ± abdominal imaging: recommended if nomogram predicts >10% probability of pelvic lymph node involvement	Not routinely recommended
Very high	• T3b-T4 OR • Primary Gleason pattern 5 OR • >4 cores with Gleason score 8–10/ grade group 4 or 5	• Bone imaging[k]: recommended • Pelvic ± abdominal imaging: recommended if nomogram predicts >10% probability of pelvic lymph node involvement	Not routinely recommended

Clinically Localized Prostate Cancer: AUA/ASTRO/SUO Guideline

Published 2017

GUIDELINE STATEMENTS

Active Surveillance- Very Low-Risk

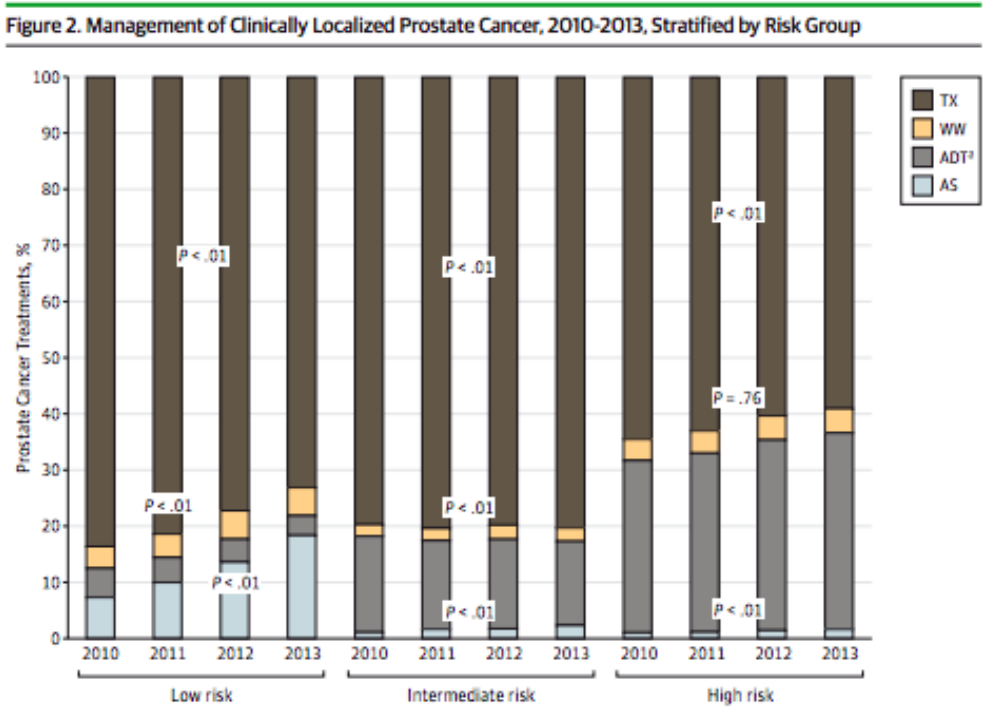
- Clinicians should recommend active surveillance as the best available care option (*Strong Recommendation; Evidence Level A*)

Active Surveillance- Low-Risk

- Clinicians should recommend active surveillance as the preferable care option (*Moderate Recommendation; Evidence Level B*)
- Clinicians may offer definitive treatment (i.e. radical prostatectomy or radiotherapy) to select patients who may have a high probability of progression (*Conditional Recommendation; Evidence Level B*)

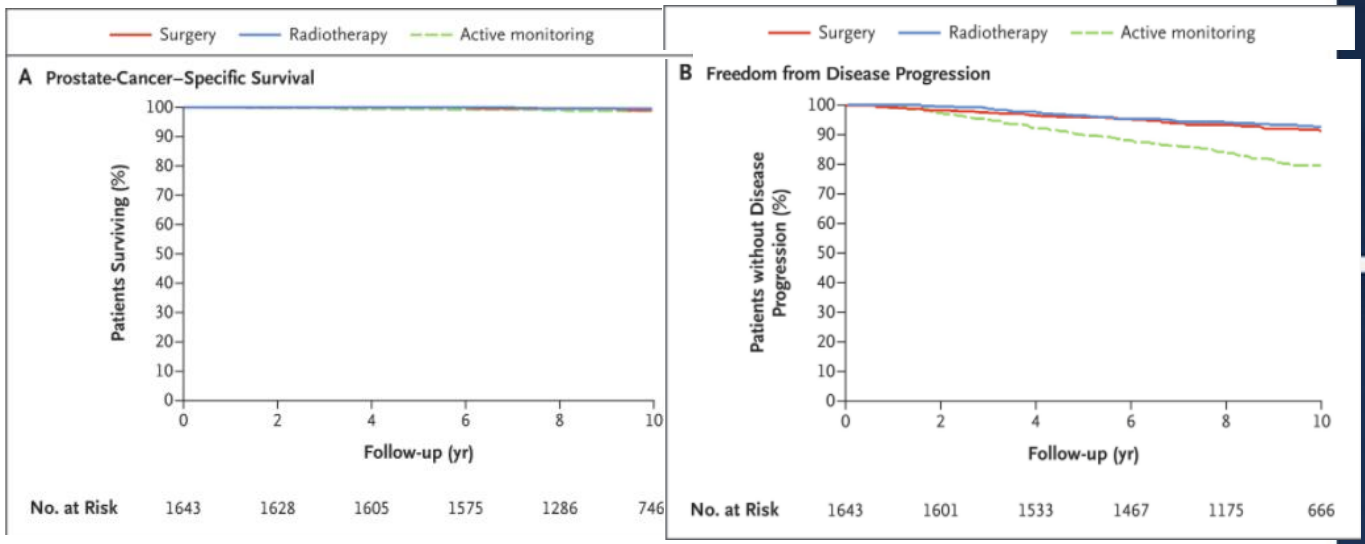
VIGILÂNCIA ATIVA

- US National Cancer Data Base



Maurice MJ, et al.. JAMA Oncol 2016;2:1505–7

- PROTECT Trial



Hamdy FC, et al.. N Engl J Med 2016;375:1415-24

Active Surveillance

Vantagens	Desvantagens
• Evita efeitos colaterais do tratamento definitivo	• Risco de progressão da doença
• Preserva QoL	• Risco de perder oportunidade de cura
	• 1/3 precisrá de tratamento

TESTE MOLECULAR TECIDUAL→ TOMADA DE DECISÃO

DECIPHER BY GENOME DX

- Teste molecular → Medicina personalizada, de precisão
- 22 biomarcadores genéticos (expressão de RNA)
  - Proliferação do ciclo celular
  - Adesão
  - Motilidade
  - Modulação imune
  - Sinalização androgênica
- Resultado 0-1
  - < 0,45 → Baixo
  - 0,45 – 0,60 → Intermediário (2x risco de metástase)
  - > 0,60 → Alto (7x risco de metástase)

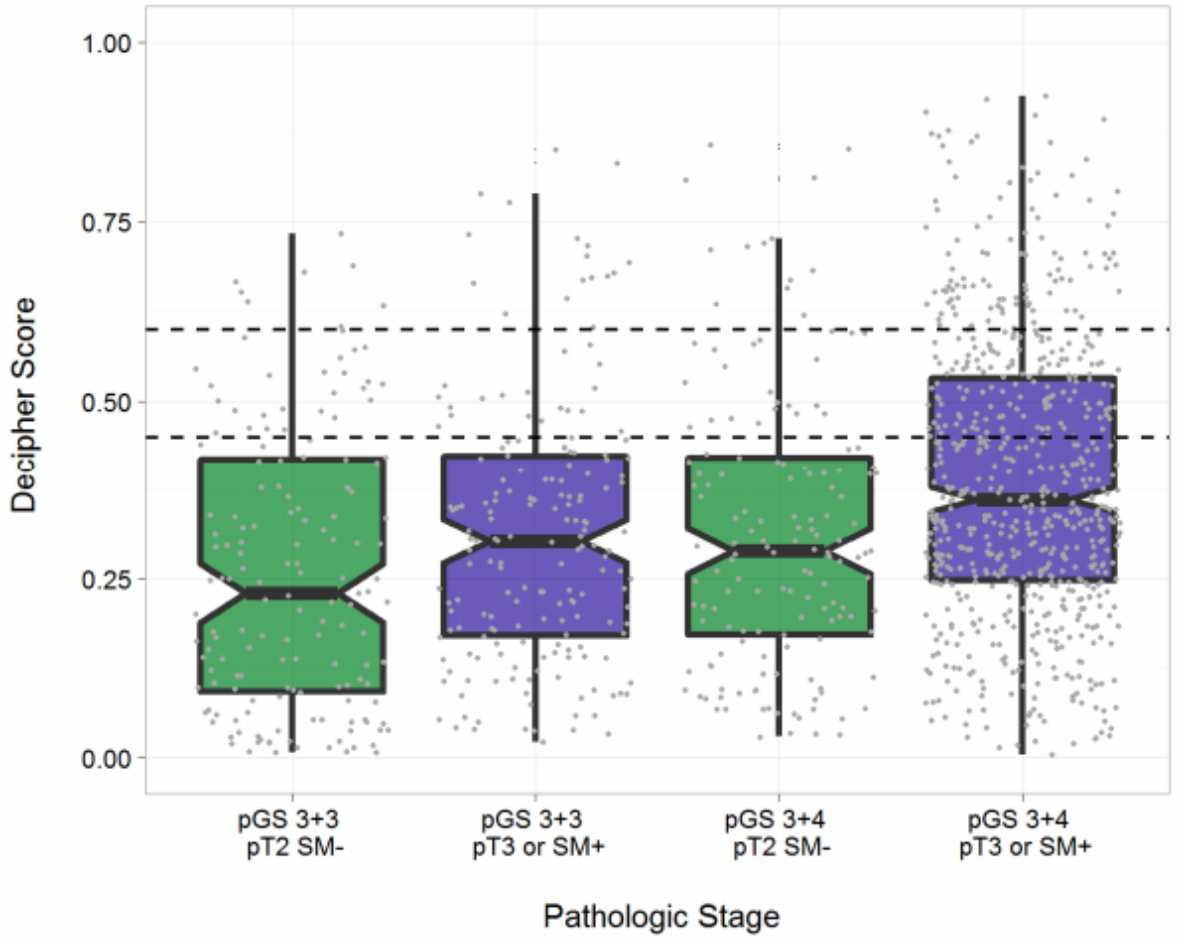
Erho N, et al. PLoS One 2013;8:e66855

THE JOURNAL of UROLOGY®
Official Journal of the American Urological Association
January 2017 Volume 197, Issue 1, Pages 122–128

Molecular Analysis of Low Grade Prostate Cancer Using a Genomic Classifier of Metastatic Potential

Eric A. Klein†, María Santiago-Jiménez†, Kasra Yousefi†, Bruce A. Robbins, Edward M. Schaeffer†, Bruce J. Trock, Jeffrey Tosoian, Zaid Haddad†, Seong Ra, R. Jeffrey Karnes, Robert B. Jenkins, John C. Cheville, Robert B. Den, Adam P. Dicker, Elai Davicioni†, Stephen J. Freedland†, Ashley E. Ross†

- Determinar % de G6 (3+3) com características moleculares de doença com potencial metastático
- 337 prostatectomias G6
  - 80% → Decipher baixo
  - 13% → Decipher intermediário
  - 7% → Decipher alto
- Decipher alto relacionado com:
  - Extensão extra-prostática
  - VVSS +
  - Margem +



Clinically Localized Prostate Cancer: AUA/ASTRO/SUO Guideline

Published 2017

GUIDELINE STATEMENTS

Standard Therapy

- Clinicians should recommend radical prostatectomy or radiotherapy plus ADT as standard treatment options for patients with high-risk localized prostate cancer (*Strong Recommendation, Evidence Level A*)

MONOTERAPIA É SUFICIENTE???

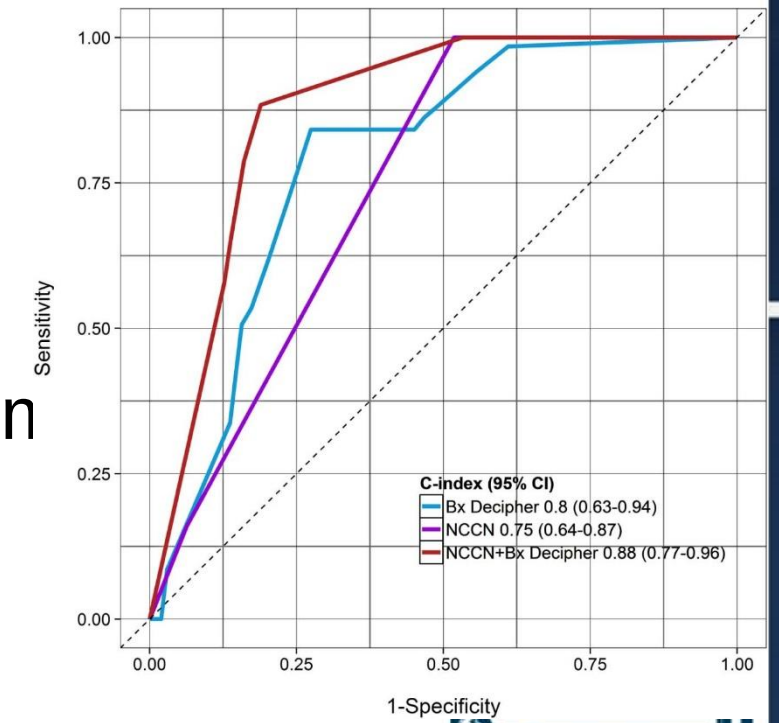
UROLOGY

April 2016 Volume 90, Pages 148–152

Decipher Genomic Classifier Measured on Prostate Biopsy Predicts Metastasis Risk

Eric A. Klein, Zaid Haddad, Kasra Yousefi, Lucia L.C. Lam, Qiqi Wang, Voleak Choeurng, Beatrix Palmer-Aronsten, Christine Buerki, Elai Davicioni, Jianbo Li, Michael W. Kattan, Andrew J. Stephenson, Cristina Magi-Galluzzi

- BxP de 57 pacientes de uma série de Decipher
  - PSA > 20 ou pT3 ou margem + ou G 8-10
- Seguimento de 8 anos
  - 8 metástases
  - 3 mortes por CaP
- Análise multivariada para desenvolvimento de n
  - Decipher (HR=1,72, para cada 10% de aumento)
  - Idade (NS)
  - PSA pré-op (NS)
  - Gleason da Bx (NS)



EUROPEAN UROLOGY
Forward faster. Together.
November 2017 Volume 72, Issue 5, Pages 845–852

Ability of a Genomic Classifier to Predict Metastasis and Prostate Cancer-specific Mortality after Radiation or Surgery based on Needle Biopsy Specimens

Paul L. Nguyen, Zaid Haddad, Ashley E. Ross, Neil E. Martin, Samineh Deheshi, Lucia L.C. Lam, Jijumon Chelliserry, Jeffrey J. Tosoian, Tamara L. Lotan, Daniel E. Spratt, Radka S. Stoyanova, Sanoj Punnen, Kaye Ong, Christine Buerki, Maria Aranes, Tyler Kolisnik, Jennifer Margrave, Kasra Yousefi, Voleak Choeurng, Elai Davicioni, Bruce J. Trock, Christopher J. Kane, Alan Pollack, John W. Davis, Felix Y. Feng†, Eric A. Klein†

- 235 pacientes de risco intermediário e alto
  - 105 prostatectomias
  - 130 Radio ± Hormonio
- Seguimento de 6 anos
  - 34 metástases
  - 11 mortes por CaP

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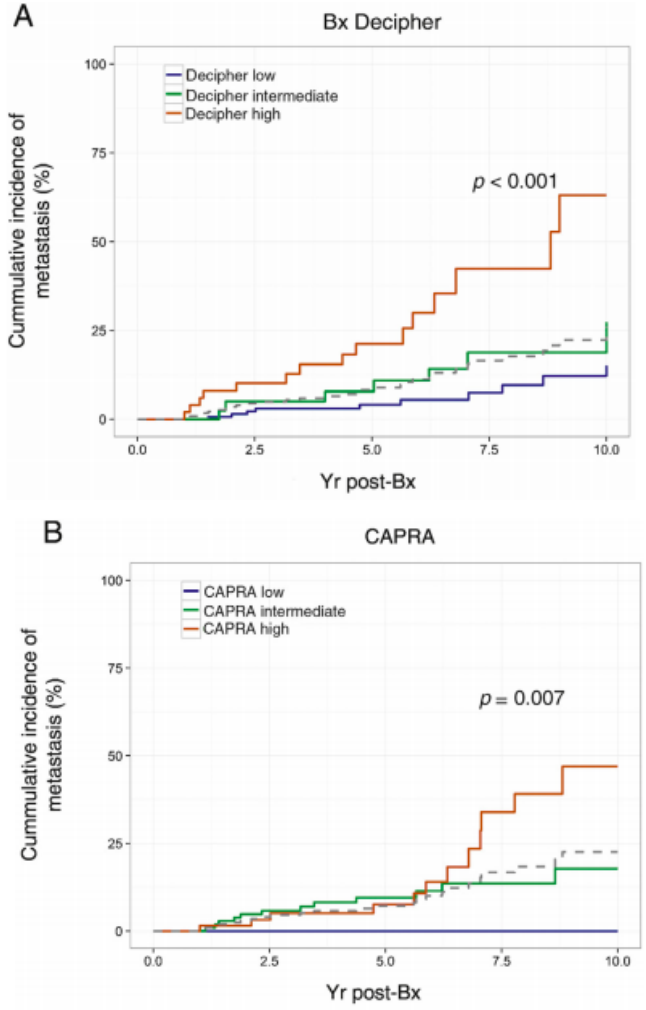
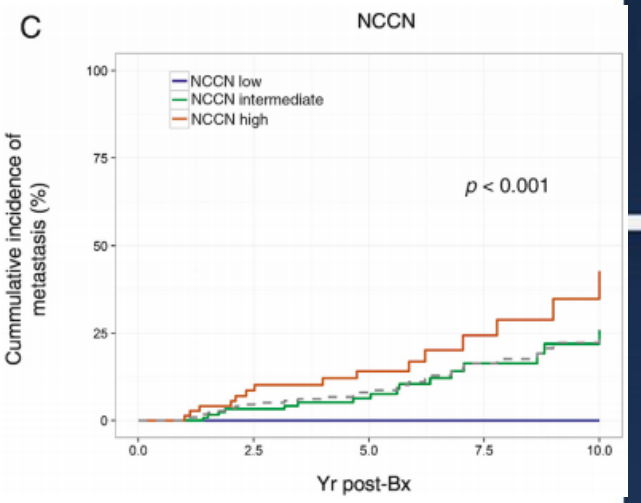
- Sobrevida livre de metástase

MVA		
Variable	Hazard ratio (95% CI)	*p* value
Patient's age at first line treatment	1.03 (0.97–1.1)	0.29
log2 Pretreatment PSA (ng/ml)	1.00 (0.68–1.48)	1
Grade Group 1	Reference	1
Grade Groups 2–3	2.80 (0.65–16.2)	0.17
Grade Groups 4–5	4.78 (0.92–32.2)	0.063
Clinical stage ≤T1c	Reference	1
Clinical stage ≥T2a	1.09 (0.42–3.06)	0.9
Bx Decipher[a]	1.39 (1.09–1.8)	0.009
First-line treatment RP	Reference	1
First-line treatment RT ± ADT	0.73 (0.26–2.28)	0.6





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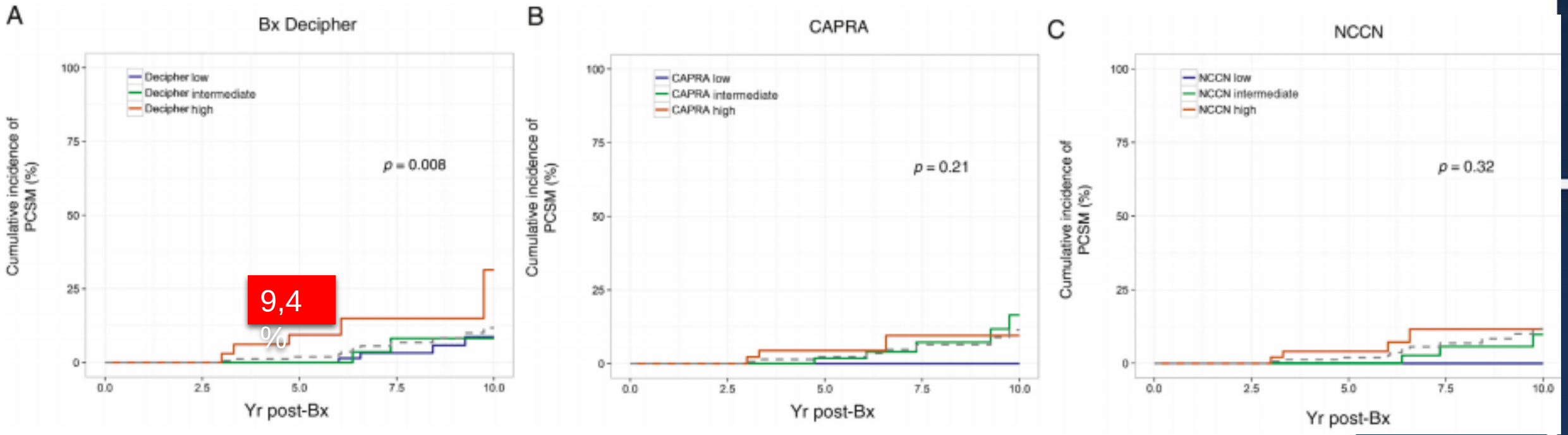
- Sobrevida Câncer-específica em 5 anos



9,4 %

HR: 1,57 (para cada aumento de 10%)

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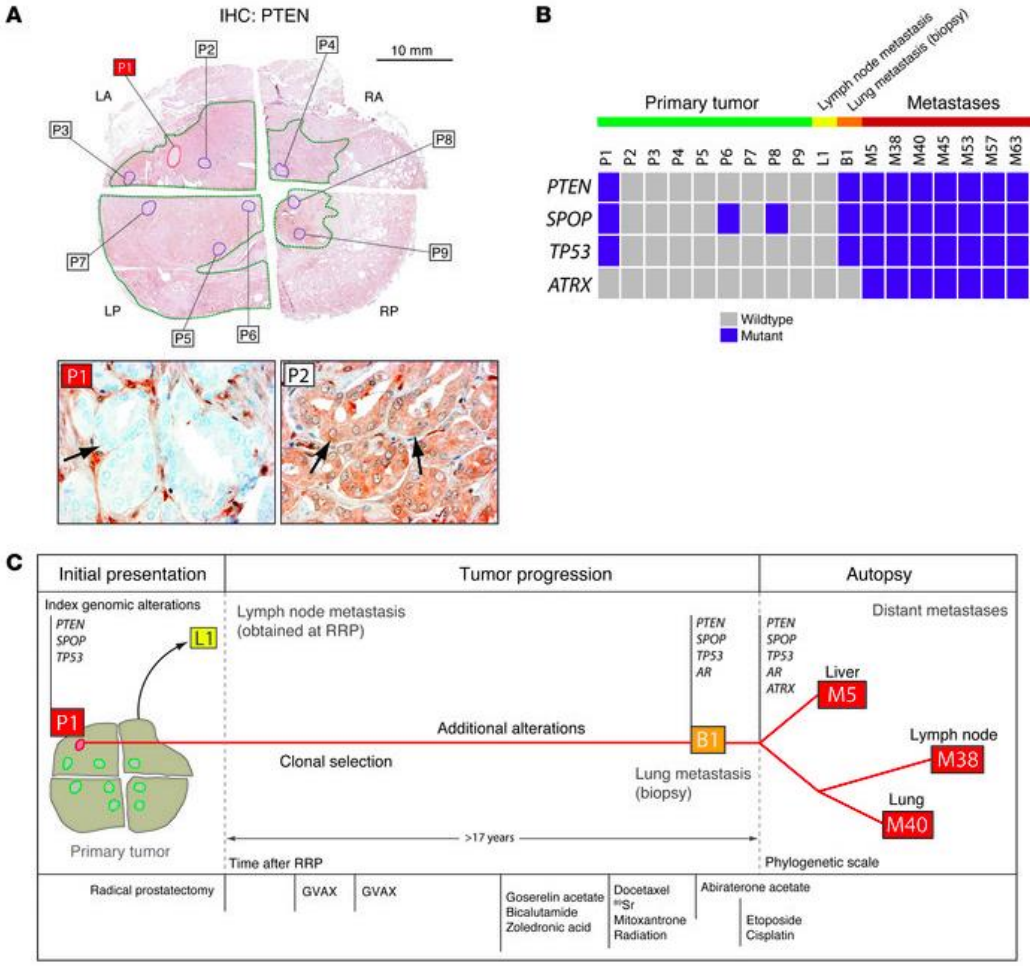
CONCLUSÃO

HISTOLOGIA ≠ BIOLOGIA MOLECULAR

Avaliação Genômica ao Diagnóstico → Prognóstico Mais Preciso → Tratamento Adequado



Haffner MC, et al. J Clin Invest 2013;123:4918-22

OBRIGADO

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1 a 3 de Março de 2018