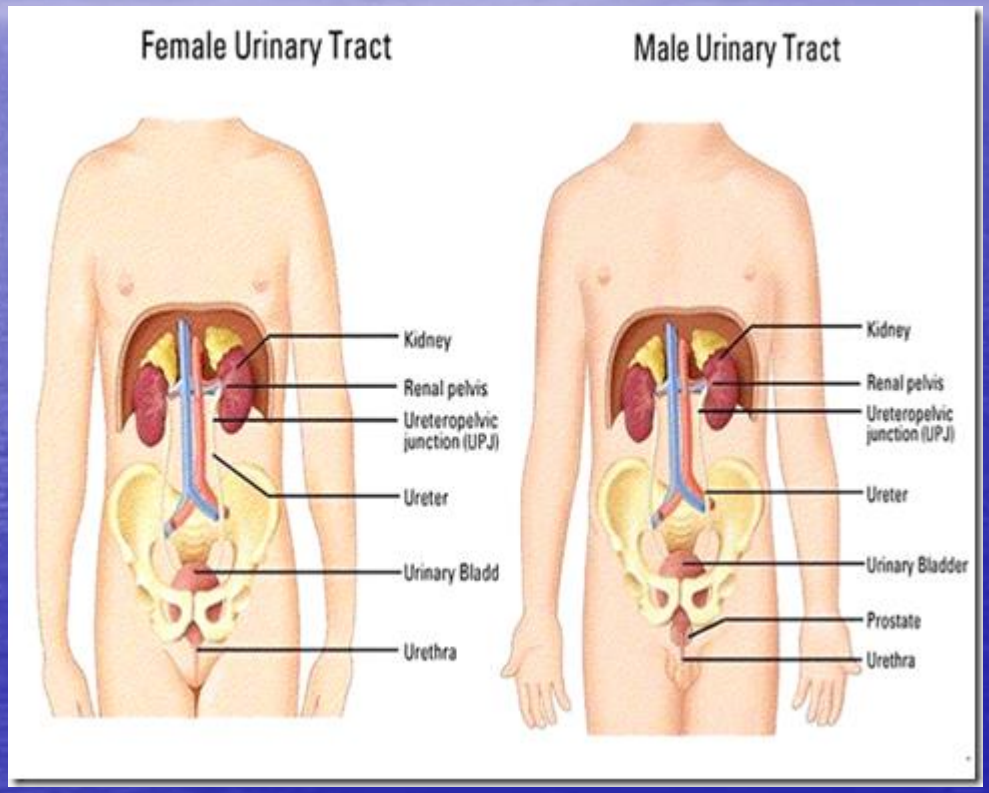
Az urológiai daganatos betegek kezelésének múltja, jelene és jövője

Bőde Imre

2015.04.30.


Female Urinary Tract
Kidney
Renal pelvis
Ureteropelvic junction (UPJ)
Ureter
Urinary Bladd
Urethra
Male Urinary Tract
Kidney
Renal pelvis
Ureteropelvic junction (UPJ)
Ureter
Urinary Bladder
Prostate
Urethra

Veserák

- **felnőttkori rosszindulatú daganatok 2-3%**
- **Mo évi 2300-2400 beteg**
- **évi 700 halál**

Húgyhólyagdaganat

- felnőttkori daganatok 2-3%
- hólyagban előforduló urothelsejtes tumor a negyedik leggyakrabban előforduló daganat
- Európában évente közel 120.000 új megbetegedés
- Hazánkban évente mintegy 2000 új húgyhólyagrákos esetet diagnosztizálnak
- Magyar Rákregiszter adatai alapján évente körülbelül 8-900 halál történik húgyhólyagrák

Prosztatarák

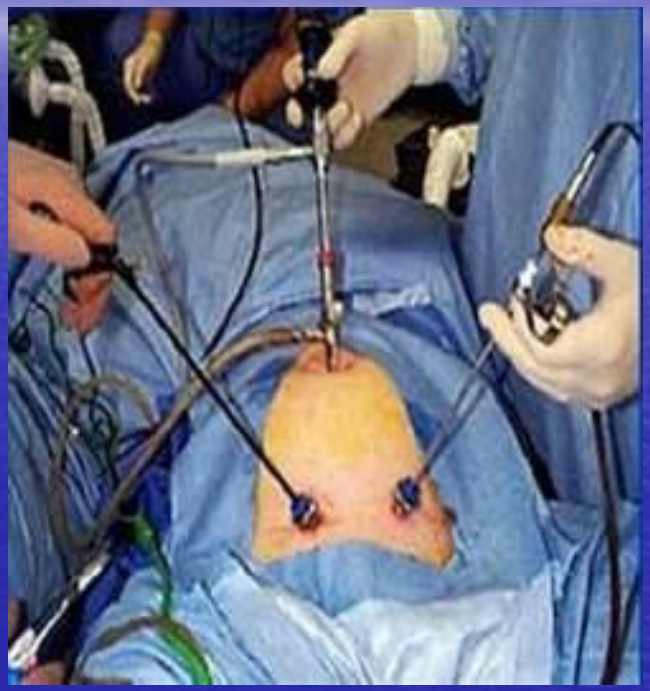
- daganatos elváltozások kb. 15 százaléka
- Nemzeti Rákregiszter: évi 3300 és 3800 felfedezés és 1500 haláleset
- világviszonylatban a férfiak körében a tüdőrák után a második leggyakrabban előforduló rosszindulatú daganat
- Európai Unió országaiban 80-90 000 új esetet

Első próbálkozások

1869, Gustav Simon – nyílt nephrectomia
1991, Ralph V. Clayman - laparoscopos nephrectomia

1905, Hugh Hampton Young, nyílt perineális prostatectomia
1947, Terence Millin, nyílt retropubikus prostatectomia
1991, W. W. Schussler, laparoscopos prostatectomia
2000, Mani Mennon, robotasszisztált prostatectomia

1910, Edwin Beer - első TUR
1951, Eugene M. Bricker - első cystectomia

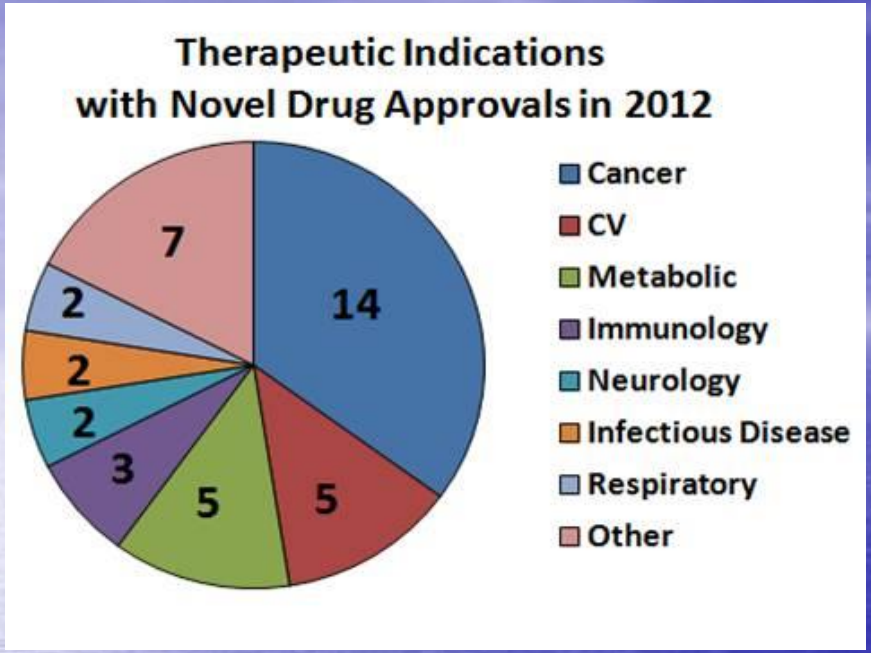


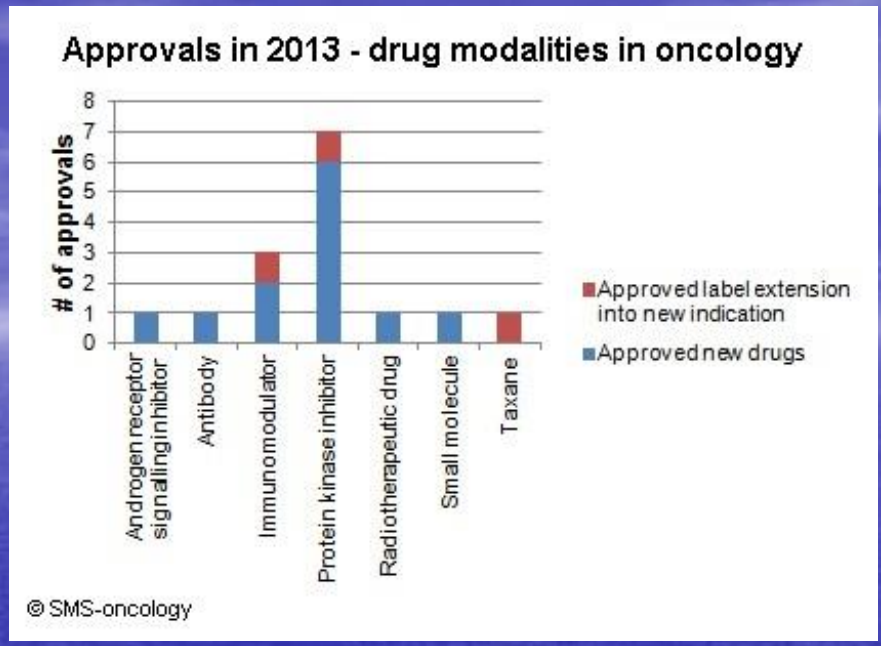
Onkológiai kezelés

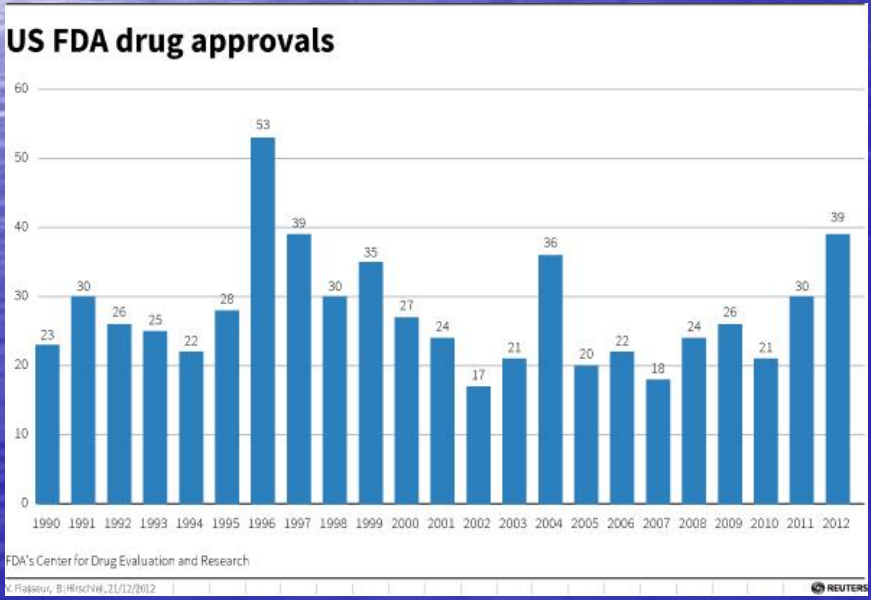
Veserák:
Interferon, Interleukin: 80-as évek
Sunitinib: 2006.01.

Húgyhólyagrák:
Felületes:
Intravezikális CHT : 1982
Intravezikális BCG: 1976

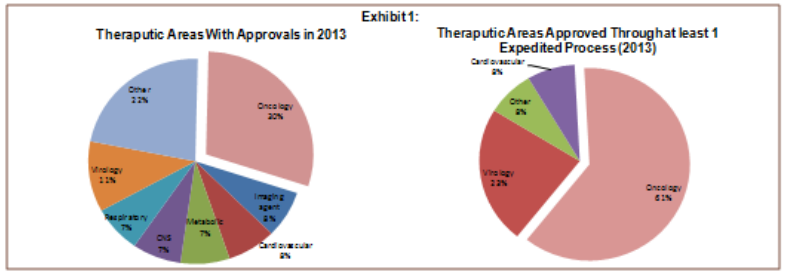
Kemotherápia:
Cisplatin: 1978
Gemcitabine: 1995







In 2013, Oncology dominated overall approvals (30%) and expedited approvals (61%)



PROSZTATARÁK

- 1966 Nobel díj, Charles Huggins
- Ösztrogén kezelés

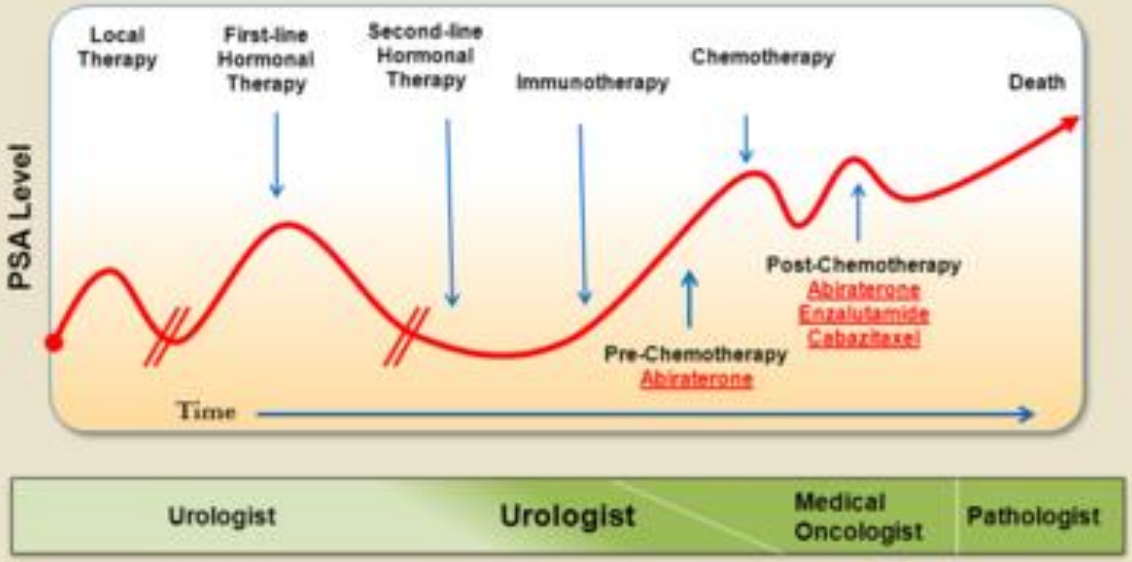
- 1985 LHRH analógok
- 2008 LHRH antagonosták

Table 1. Summary of current treatment options for metastatic castration-resistant prostate cancer

Study	Regimen and no. of patients	Patient characteristics	Hazard ratio	Survival time (mo)
TAX 327 [33]	Docetaxel plus prednisone every 3 weeks ($n = 335$), weekly ($n = 334$) or mitoxantrone plus prednisone ($n = 337$)	CRPC, chemotherapy naïve	0.76	18.9 vs. 16.5
COU-AA-302[a] [36, 37]	Abiraterone acetate plus prednisone ($n = 546$) vs. placebo plus prednisone ($n = 542$)	CRPC, chemotherapy naïve, asymptomatic/ mildly symptomatic	0.79	35.3 vs. 30.1
IMPACT[b] [38]	Sipuleucel-T ($n = 341$) vs. placebo ($n = 171$)	CRPC, chemotherapy naïve, asymptomatic/ minimally symptomatic	0.78	25.8 vs. 21.7
TROPIC [29]	Cabazitaxel plus prednisone ($n = 378$) vs. mitoxantrone plus prednisone ($n = 377$)	CRPC, postdocetaxel	0.70	15.1 vs. 12.7
COU-AA-301 [30, 31]	Abiraterone acetate plus prednisone ($n = 797$) vs. placebo plus prednisone ($n = 398$)	CRPC, postdocetaxel	0.74	15.8 vs. 11.2
AFFIRM[b] [28]	Enzalutamide ($n = 800$) vs. placebo ($n = 399$)	CRPC, postdocetaxel	0.63	18.4 vs. 13.6
ALSYMPCA[a] [32]	Radium-223 ($n = 614$) vs. placebo ($n = 307$)	CRPC, postdocetaxel or unfit for docetaxel	0.69	14.9 vs. 11.3

[a]Not yet approved in European Union or U.S.
[b]Not yet approved in European Union.
Abbreviation: CRPC, castration-resistant prostate cancer.

Natural History of Prostate Cancer



Treatment Landscape

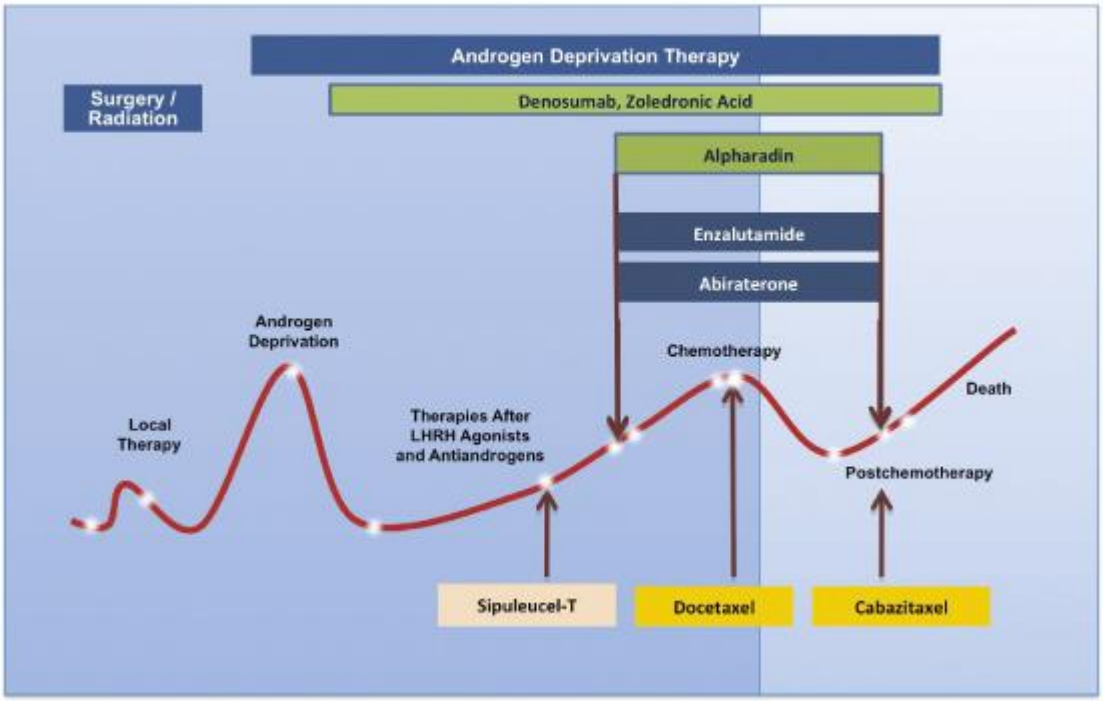
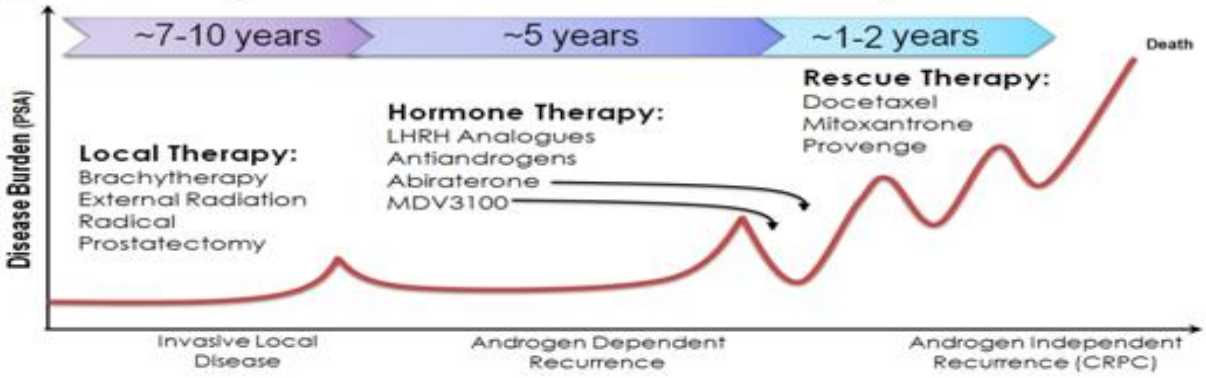
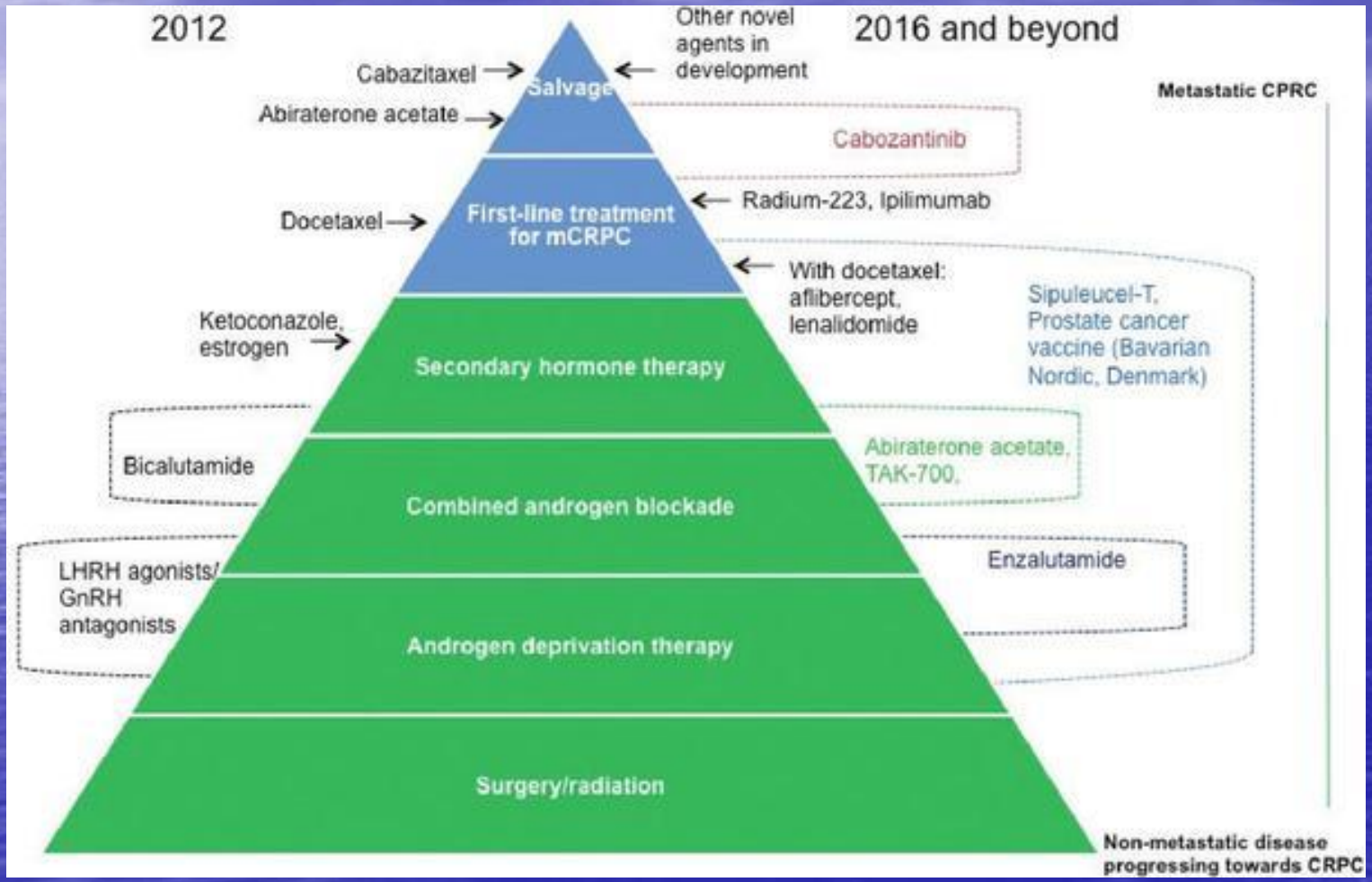
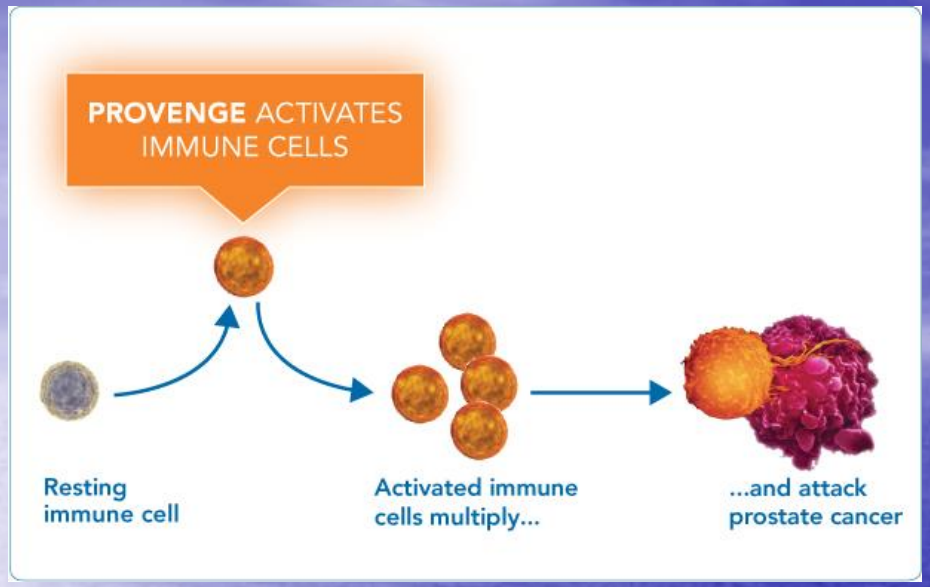
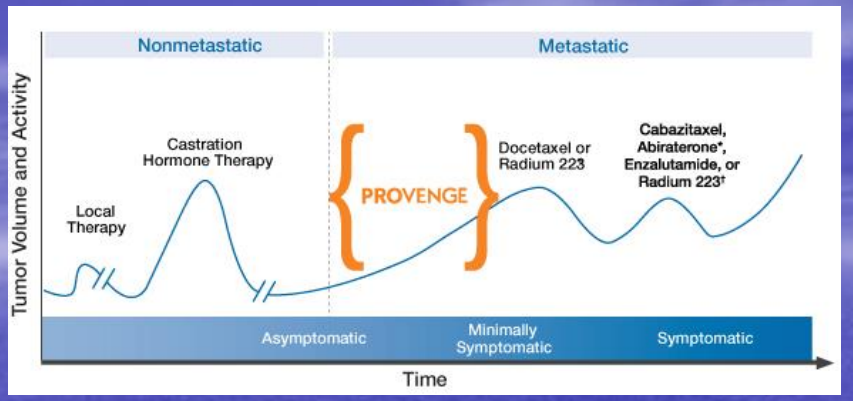


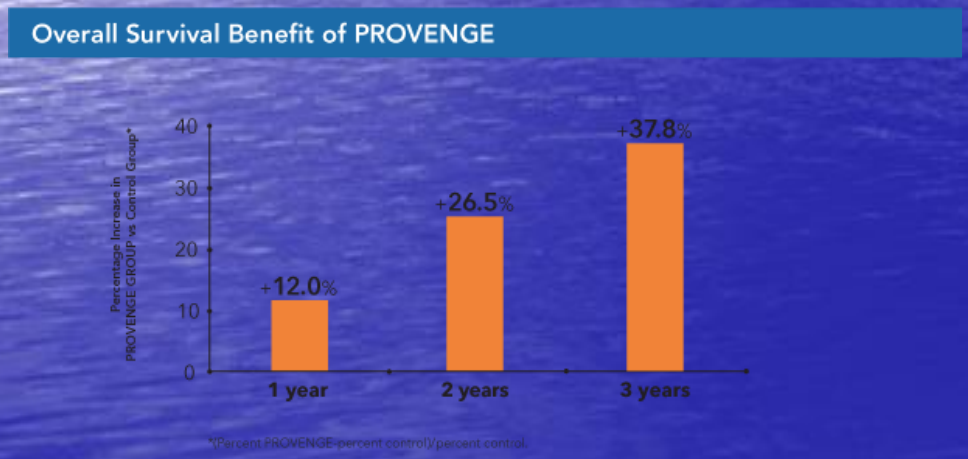
Figure 2 ***Typical Recurrent Prostate Cancer Outcome***

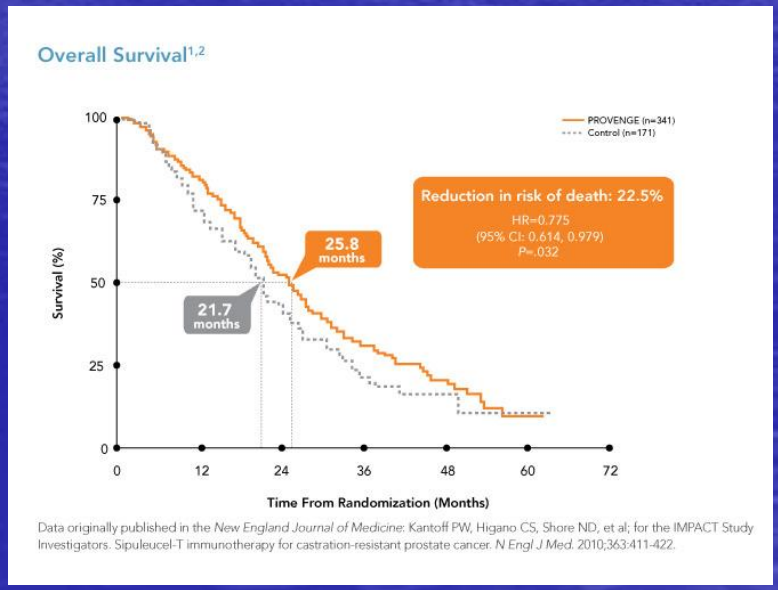



2012
2016 and beyond
Other novel agents in development
Cabazitaxel
Abiraterone acetate
Salvage
Metastatic CPRC
Cabozantinib
Docetaxel
First-line treatment for mCRPC
Radium-223, Ipilimumab
With docetaxel: aflibercept, lenalidomide
Sipuleucel-T, Prostate cancer vaccine (Bavarian Nordic, Denmark)
Ketoconazole, estrogen
Secondary hormone therapy
Bicalutamide
Abiraterone acetate, TAK-700,
Combined androgen blockade
Enzalutamide
LHRH agonists/ GnRH antagonists
Androgen deprivation therapy
Surgery/radiation
Non-metastatic disease progressing towards CRPC

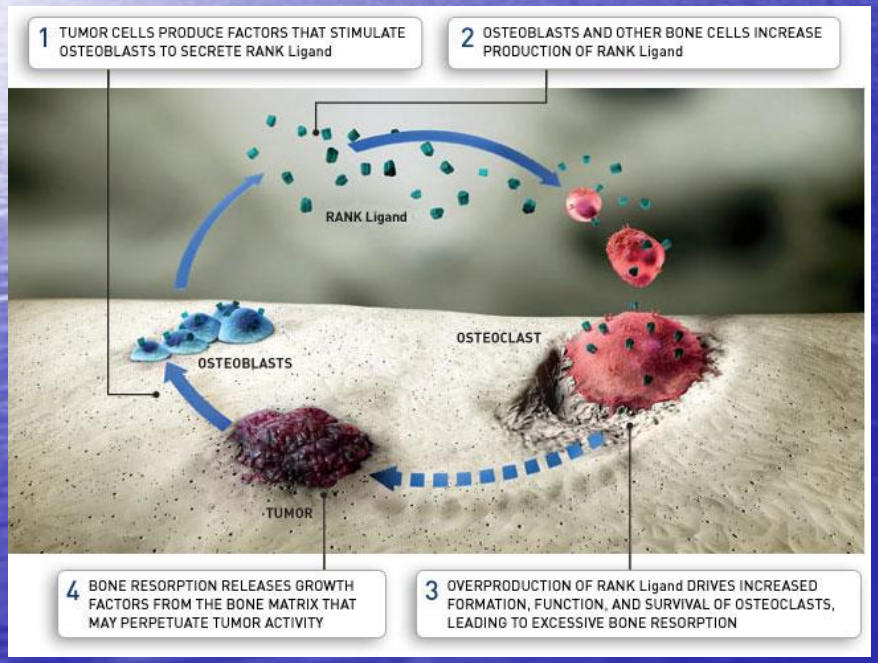

PROVENGE ACTIVATES IMMUNE CELLS
Resting immune cell
Activated immune cells multiply...
...and attack prostate cancer

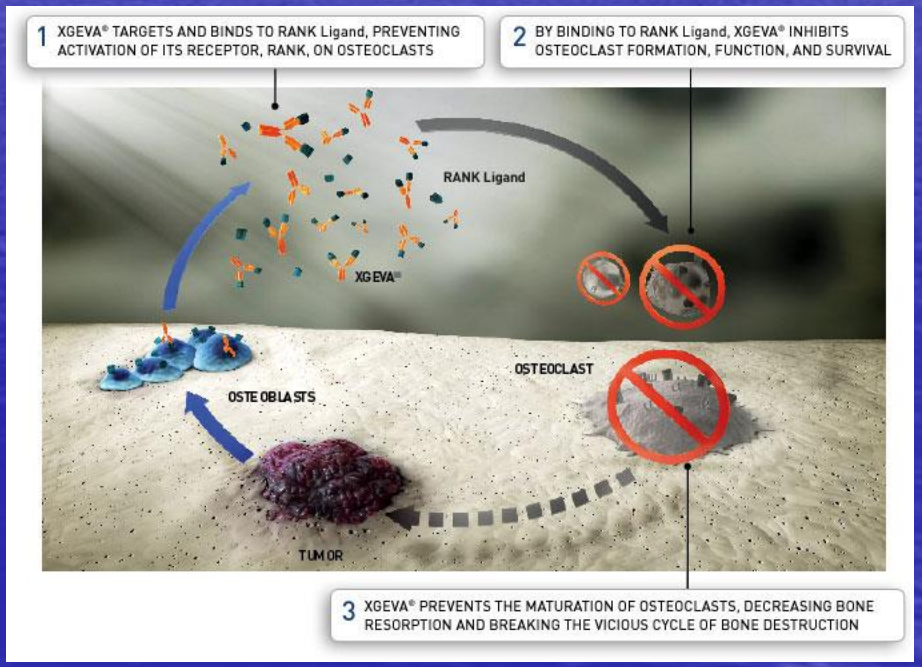

Nonmetastatic
Metastatic
Tumor Volume and Activity
Local Therapy
Castration Hormone Therapy
PROVENGE
Docetaxel or Radium 223
Cabazitaxel, Abiraterone*, Enzalutamide, or Radium 223†
Asymptomatic
Minimally Symptomatic
Symptomatic
Time


Overall Survival Benefit of PROVENGE
Percentage Increase in PROVENGE GROUP vs Control Group*
40
30
20
10
0
+12.0%
+26.5%
+37.8%
1 year
2 years
3 years
*(Percent PROVENGE-percent control)/percent control.


Overall Survival[1,2]
PROVENGE (n=341)
Control (n=171)
Reduction in risk of death: 22.5%
HR=0.775
(95% CI: 0.614, 0.979)
P=.032
25.8 months
21.7 months
Survival (%)
100
75
50
25
0
0
12
24
36
48
60
72
Time From Randomization (Months)
Data originally published in the New England Journal of Medicine: Kantoff PW, Higano CS, Shore ND, et al; for the IMPACT Study Investigators. Sipuleucel-T immunotherapy for castration-resistant prostate cancer. N Engl J Med. 2010;363:411-422.

DENOSUMAB


1 TUMOR CELLS PRODUCE FACTORS THAT STIMULATE OSTEOBLASTS TO SECRETE RANK Ligand
2 OSTEOBLASTS AND OTHER BONE CELLS INCREASE PRODUCTION OF RANK Ligand
RANK Ligand
OSTEOBLASTS
OSTEOCLAST
TUMOR
4 BONE RESORPTION RELEASES GROWTH FACTORS FROM THE BONE MATRIX THAT MAY PERPETUATE TUMOR ACTIVITY
3 OVERPRODUCTION OF RANK Ligand DRIVES INCREASED FORMATION, FUNCTION, AND SURVIVAL OF OSTEOCLASTS, LEADING TO EXCESSIVE BONE RESORPTION


1 XGEVA® TARGETS AND BINDS TO RANK Ligand, PREVENTING ACTIVATION OF ITS RECEPTOR, RANK, ON OSTEOCLASTS
2 BY BINDING TO RANK Ligand, XGEVA® INHIBITS OSTEOCLAST FORMATION, FUNCTION, AND SURVIVAL
RANK Ligand
XGEVA®
OSTEOCLAST
OSTEOBLASTS
TUMOR
3 XGEVA® PREVENTS THE MATURATION OF OSTEOCLASTS, DECREASING BONE RESORPTION AND BREAKING THE VICIOUS CYCLE OF BONE DESTRUCTION

More Options Than Ever for Treatment of Metastatic CRPC Patients

Regimen	Approval Year	Improved Survival	Hazard Ratio
Docetaxel / pred[9]	2004	2.9 months	0.79
Sipuleucel –T[10]	2010	4.1 months	0.77
Cabazitaxel/pred[11]	2010	2.4 months	0.70
Abiraterone/pred[12]	2011	4.6 months	0.74
Enzalutamide[13]	2012	4.8 months	0.63
Radium 223[14]	2012	3.6 months	0.69
Total		22.4 months	

(For references, see text.)

KÖSZÖNÖM A FIGYELMET!