IPOGONADISMO,
PATOLOGIA PROSTATICA
E DISFUNZIONI SESSUALI:
Endocrinologo ed Urologo a confronto

28 SETTEMBRE 2018
MILANO

Ripercussioni sistemiche ed andrologiche della deprivazione androgenica

Dr. Emanuele Ferrante
UOC Endocrinologia – Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico di Milano
emanuele.ferrante@policlinico.mi.it

ADT & Disfunzione sessuale

Sexual Dysfunction				
Loss of libido/sexual interest/drive	58.0[d]	299	—	Potosky et al, 2001[31]
	69.0[g]	170	29	Fowler et al, 2002[44]
	91.4[c]	111	74	Ng et al, 2012[43]
Adverse Effects	**Prevalence Rate[a](%)**	**Sample Size**	**Comparison Group[b]**	**Source**
Erectile dysfunction/impotence	73.3[d]	299	—	Potosky et al, 2001[31]
	85.0[c]	97	57	Ng et al, 2012[43]
	95.0[g]	166	77	Fowler et al, 2002[44]
Cessation of sexual activity	80.2[d]	299	—	Potosky et al, 2001[31]
	93.0[c]	111	56	Ng et al, 2012[43]

1. **Ridotta risposta tissutale ai vasodilatatori (↓inflow)**
2. **Ridotta compliance tissutale (↑outflow)**

Walker LM et al, CGC 2013

ADT & Disfunzione sessuale

Problem	Intervention	Study	Patients, *n*	Outcome
Sexual dysfunction	Intermittent ADT	Crook et al. [73]	1386	Increased libido; no decrease in survival compared with continuous ADT in nonmetastatic men
		Hussain et al. [74]	1535	Increased erectile function, but treatment failed noninferiority for survival in metastatic patients
	Aerobic and resistance exercise	Cormie et al. [77]	57	Maintained sexual activity and interest in sex
Gynecomastia	Breast radiation	Widmark et al. [80]	253	Significant reduction in gynecomastia
		Tyrrell et al. [78]	106	
	Tamoxifen	Boccardo et al. [81]	114	
	Breast radiation vs tamoxifen	Di Lorenzo et al. [82]	102	RT and tamoxifen both reduce gynecomastia compared with observation, but tamoxifen reduces it more

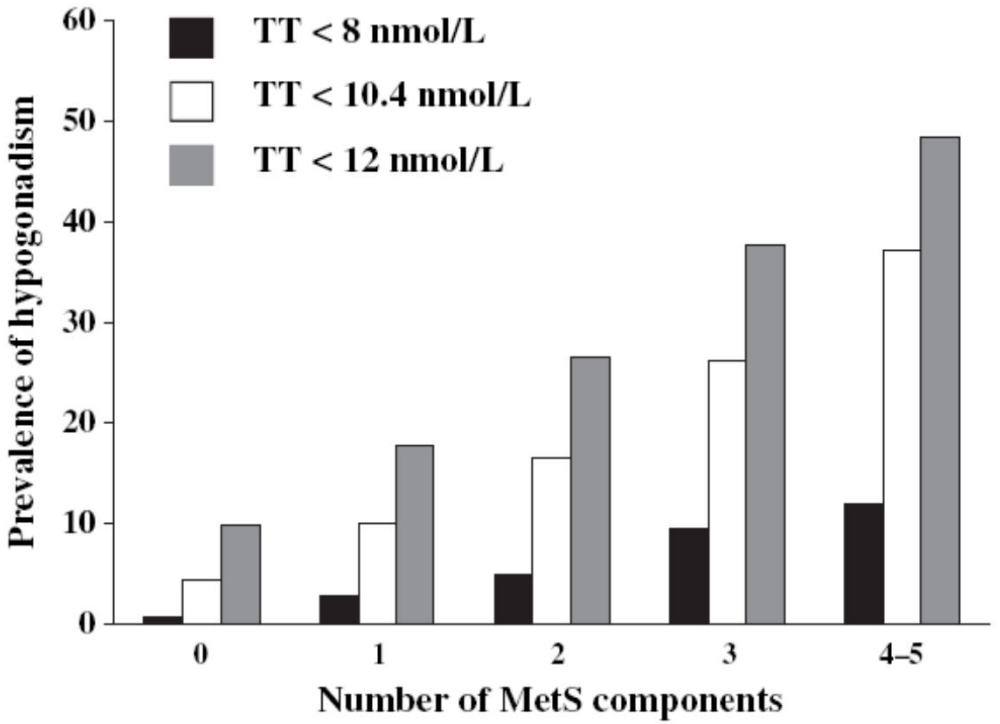
Adverse Effects	Pre-ADT prevalence, %	Risks	Monitoring	Treatment
Sexual dysfunction: loss of libido, erectile dysfunction	15–70	60–90%	As required	Counselling and referral to psychosocial and/or sexual rehabilitation experts Phosphodiesterase inhibitors (non-Pharmaceutical Benefits Scheme) Intracavernosal injections (non- Pharmaceutical Benefits Scheme) Penile pump and prosthesis

Rhee H et al, BJUI 2015

Nguyen PL et al, Eur Urol 2014

Ipogonadismo & Sindrome Metabolica

NCEP-ATP III (2001)	IDF (2005)
National Cholesterol Education Program	**International Diabets Federation**
▪ Circonferenza vita ≥102 cm	1. Circonferenza vita ≥94 cm
▪ Pressione arteriosa >130/85 mmHg	▪ Pressione arteriosa >130/85 mmHg
▪ Trigliceridi ≥150 mg/dl (≥ 2.3 mmol/L)	▪ Trigliceridi ≥150 mg/dl (≥ 2.3 mmol/L)
▪ HDL <40 mg/dl (<1.03 mmol/L)	▪ HDL <40 mg/dl (<1.03 mmol/L)
▪ Glicemia a digiuno ≥110 mg/dl (≥6.1 nmol/L)	▪ Glicemia a digiuno ≥100 mg/dl (≥5.5 nmol/L)
Diagnosi: ≥ 3 criteri	Diagnosi: criterio 1 + 2 dei 4 rimanenti +/- Criteri aggiuntivi: HOMA>2.4, incremento citochine e chemochine infiammatorie (PCR , IL-6, NFKB) ed adipochine (leptina, TNF-α, PAI-1, angiotensinogeno)



Corona et al 2008, Int J Androl

ADT & Sindrome Metabolica

	wk 0	wk 12	Change, %	*P* value
Total cholesterol (mg/dl)[a]	172 ± 6	187 ± 7	+9.4 ± 2.4	<0.001
HDL cholesterol (mg/dl)[b]	52 ± 3	57 ± 3	+9.9 ± 2.9	0.01
LDL cholesterol (mg/dl)[c]	100 ± 6	107 ± 7	+8.7 ± 4.7	0.09
Triglycerides (mg/dl)[d]	98 ± 9	115 ± 9	+23.0 ± 8.0	0.04

Table 2. Prevalence of Metabolic Syndrome and Its Components in All Groups

	ADT Group (n = 20)		Non-ADT Group (n = 18)		Controls (n = 20)		
Condition	No. of Patients	%	No. of Patients	%	No. of Patients	%	Overall *P*
Metabolic syndrome	11	55	4	22	4	20	.03
Waist > 40 inches	15	75	6	33	6	30	.007
Glucose > 110 mg/dL	13	65	3	16	6	30	.006
Triglycerides ≥ 150 mg/dL	11	55	8	44	4	20	.06
HDL < 40 mg/dL	7	35	9	50	10	50	.55
Hypertension	9	45	5	28	8	40	.53

Abbreviations: ADT, androgen-deprivation therapy; HDL, high-density lipoprotein.

Smith MR et al, JCEM 2006

Braga-Basaria M et al, JCO 2006

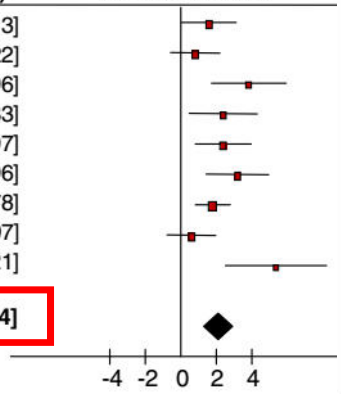
ADT & Sindrome Metabolica

% of change in body weight

Studies	Number of patients	Duration (month)	Study weight	Change in percentage (95% CI)
Berruti et al (18)	35	12	12.0%	1.60 [0.07, 3.13]
Nishiyama et al (23)	42	6	12.9%	0.83 [-0.56, 2.22]
Nowicki et al (24)	18	3	8.5%	3.84 [1.72, 5.96]
Smith et al (25)	22	3	9.5%	2.41 [0.49, 4.33]
Smith et al (27)	32	12	11.7%	2.40 [0.83, 3.97]
Smith et al (17)	26	12	10.4%	3.20 [1.44, 4.96]
Smith et al (26)	79	12	16.2%	1.80 [0.82, 2.78]
Smith et al (28)	25	3	13.1%	0.60 [-0.77, 1.97]
Tayek et al (29)	10	12	5.7%	5.37 [2.53, 8.21]
Total (95% CI)			**100.0%**	**2.14 [1.35, 2.94]**

Heterogeneity: Chi² = 17.59, df = 8 (P = 0.02); I² = 55%
Test for overall effect: Z = 5.30 (P < 0.00001)

Mean Difference 95% CI Random

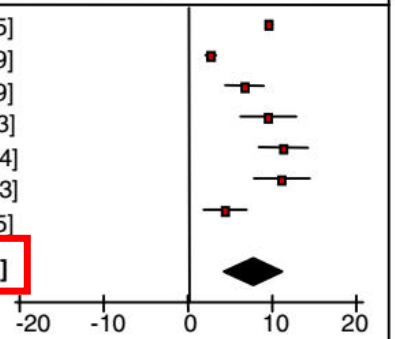


% of change in fat mass

Studies	Number of patients	Duration (month)	Study weight	Change in percentage (95% CI)
Boxer et al (19)	30	6	15.4%	9.50 [9.25, 9.75]
Galvo et al (21)	68	9	15.3%	2.60 [2.01, 3.19]
Lee et al (22)	65	12	14.4%	6.60 [4.31, 8.89]
Smith et al (27)	32	12	13.4%	9.40 [6.07, 12.73]
Smith et al (17)	26	12	13.8%	11.20 [8.26, 14.14]
Smith et al (26)	79	12	13.4%	11.00 [7.67, 14.33]
Smith et al (28)	25	3	14.2%	4.30 [1.75, 6.85]
Total (95% CI)			**100.0%**	**7.71 [4.27, 11.15]**

Heterogeneity: Chi² = 463.85, df = 6 (P < 0.00001); I² = 99%
Test for overall effect: Z = 4.40 (P < 0.0001)

Mean Difference 95% CI, Random

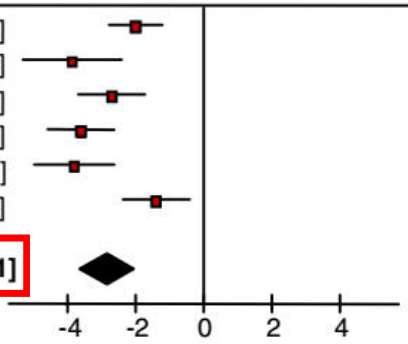


% of change in lean mass

Studies	Number of patients	Duration (month)	Study weight	Change in percentage (95% CI)
Lee et al (22)	65	12	19.1%	-2.00 [-2.78, -1.22]
Sieber et al (30)	33	24	13.3%	-3.86 [-5.31, -2.41]
Smith et al (27)	32	12	17.3%	-2.70 [-3.68, -1.72]
Smith et al (17)	26	12	17.3%	-3.60 [-4.58, -2.62]
Smith et al (26)	79	12	15.6%	-3.80 [-4.98, -2.62]
Smith et al (28)	25	3	17.3%	-1.40 [-2.38, -0.42]
Total (95% CI)			**100.0%**	**-2.82 [-3.64, -2.01]**

Heterogeneity: Chi² = 18.86, df = 5 (P = 0.002); I² = 73%
Test for overall effect: Z = 6.80 (P < 0.00001)

Mean Difference 95% CI, Random



Haseen et al, JCS 2010

ADT & metabolismo glucidico

25 pazienti trattati con GnRH analoghi per 12 settimane

	wk 0	wk 12	Change, %	*P* value
Glycoslyated hemoglobin (%)	5.46 ± 0.09	5.62 ± 0.09	+2.9 ± 0.8	<0.001
Fasting plasma glucose (mg/dl)	93 ± 2	95 ± 2	+2.0 ± 1.4	0.20
2-h plasma glucose (mg/dl)	128 ± 7	126 ± 9	+4.4 ± 7.5	0.84
Fasting plasma insulin (mU/liter)	13.5 ± 0.9	17.0 ± 2.0	+25.9 ± 9.3	0.04
Whole-body ISI (18)	3.4 ± 0.4	2.8 ± 0.3	-12.9 ± 7.6	0.02
HOMA IR (19)	7.1 ± 0.9	5.9 ± 0.6	-12.8 ± 5.9	0.02
CIR (20)	0.67 ± 0.8	0.78 ± 0.8	+30.8 ± 13.5	0.12

1. **Riduzione della sensibilità insulinica**
2. **Aumento dei livelli di insulina basale**

Smith MR et al, JCEM 2006

ADT & diabete mellito

73196 pazienti, >66 anni
Tipi di ADT:
- **GnRH analoghi**
- **Orchiectomia bilaterale**

Treatment	Incident Diabetes		
	Adjusted HR	95% CI	*P*
No treatment	Ref		—
GnRH agonist	1.44	1.34 to 1.55	< .001
Orchiectomy	1.34	1.20 to 1.50	< .001

Duration of Current GnRH Agonist Treatment (months)*	Incident Diabetes		
	Adjusted HR	95% CI	*P*
None	Ref		—
1-4	1.29	1.12 to 1.49	< .001
5-12	1.45	1.30 to 1.61	< .001
13 to 24	1.54	1.35 to 1.76	< .001
≥ 25	1.49	1.30 to 1.71	< .001

Keating NL et al, JCO 2006

37443 pazienti
Tipi di ADT:
- **GnRH analoghi**
- **Antiandrogeni orali**
- **GnRH+AA**
- **Orchiectomia bilaterale**

Treatment	**Diabetes**
No androgen deprivation therapy	Reference
GnRH agonist	1.28 (1.19 to 1.38)
Orchiectomy	1.16 (0.87 to 1.54)
Combined androgen blockade	1.17 (0.96 to 1.42)
Oral antiandrogen	1.02 (0.72 to 1.45)

Keating NL et al, JNCI 2010

ADT & DM

- I fattori di rischio tradizionali per DMT2 non modificano il rischio attribuibile alla ADT

Characteristic	Adjusted hazard ratio for association of comorbidity with myocardial infarction with or without ADT (95% CI)*		P value f interactio comorbidit ADT
	No ADT	ADT	
No comorbidity	1.00	**1.33 (1.27–1.39)**	-
Comorbidity			
Myocardial infarction	**1.29 (1.25–1.35)**	**1.32 (1.24–1.42)**	.58
Congestive heart failure	**1.34 (1.27–1.42)**	**1.35 (1.23–1.48)**	.94
Peripheral arterial disease	**1.15 (1.08–1.22)**	1.07 (0.95–1.19)	.26
Stroke	**1.13 (1.07–1.20)**	1.09 (0.98–1.22)	.60
Hypertension	**1.16 (1.11–1.20)**	**1.18 (1.10–1.26)**	.57
Obesity	**2.03 (1.86–2.21)**	**2.06 (1.74–2.44)**	.85
Chronic obstructive pulmonary disease	**1.14 (1.08–1.19)**	1.08 (0.99–1.18)	.32
Chronic renal insufficiency	**1.19 (1.10–1.28)**	1.06 (0.92–1.22)	.17
Liver disease	1. 09 (0.85–1.40)	1.32 (0.89–1.98)	.42
Peptic ulcer disease	0.96 (0.87–1.06)	1.12 (0.94–1.34)	.13
Rheumatologic disease	1.12 (0.98–1.27)	**1.26 (1.00–1.59)**	.39
Dementia	**0.79 (0.69–0.90)**	0.85 (0.68–1.06)	.57
Paralysis	0.94 (0.81–1.11)	0.89 (0.67–1.20)	.75

Keating NL et al, Eur Urol 2013

ADT & compenso in DMT2

	ADT (N=2237)				No ADT (N=2237)				
	Events	Person-years	Rate	(95% CI)	Events	Person-years	Rate	(95% CI)	*P* value†
Initiation of a diabetic medication	189	696.2	271.4	235.4-313.1	180	713.1	252.4	218.1-292.1	0.45
Addition of a new diabetes drug class	749	3076.8	243.4	226.6-261.5	652	3255.4	200.3	185.4-216.3	<0.001
Initiation or addition of a diabetes drug class	938	3773.0	248.6	233.2-265.0	832	3968.5	209.6	195.9-224.4	<0.001

Change in HbA1c over time for men with and without ADT treatment

	N	Baseline HbA1c		One Year HbA1c		Change in HbA1c from baseline to 1 year		Difference	*P* Value
1 Year									
		HbA1c, %	SE	HbA1c, %	SE	ΔHbA1c, %	SE		
ADT	2105	7.24	0.05	7.38	0.04	0.13	0.07	0.24	0.008
No ADT	2111	7.24	0.04	7.14	0.04	-0.11	0.04	Reference	-
	N	Baseline HbA1c		Two Year HbA1c		Change in HbA1c from baseline to 2 years		Difference	*P* Value
2 Years									
		HbA1c, %	SE	HbA1c, %	SE	ΔHbA1c, %	SE		
ADT	1504	7.25	0.06	7.35	0.05	0.10	0.08	0.18	0.03
No ADT	1504	7.24	0.05	7.16	0.06	-0.08	0.06	Reference	-

ADT e complicanze DMT2

- 5336 pazienti con DMT2 già presente alla dg di PC
- PC localizzato

Table 2 Risk of diabetes complications associated with ADT use, among men diagnosed with localized prostate cancer, who received primary treatment with RP or RT

Post-diagnostic diabetes complications	Event rate per 1,000 person years in ADT users	Event rate per 1,000 person years in ADT non-users	Unadjusted HR (95% CIs)	Adjusted HR[a] (95% CIs)
Any complication	249.3	231.9	1.26 (1.17–1.37)	1.12 (1.03–1.23)
Diabetic cataracts	153	136.6	1.27 (1.16–1.38)	0.98 (0.90–1.08)
Diabetic neuropathy	75.8	76.9	1.23 (1.11–1.36)	1.14 (1.02–1.28)
Diabetic retinopathy	12.7	24.8	0.63 (0.52–0.77)	1.17 (0.92–1.47)
Diabetic amputation	4.3	1.9	2.20 (1.45–3.35)	2.06 (1.28–3.31)

Aumentato (moderato!) rischio del 12% per tutte le complicanze

Bradley MC et al, CC&C 2018

ADT & rischio CV: studi osservazionali

Table 1
Observational studies evaluating the association between GnRH agonists and CV outcomes in men with PCa

Study	Database (years included)	Population	Control group	ADT type	Outcome	Adjusted HR (95% CI)[a]
Keating et al. [9]	SEER (1992–1999)	73,196 Men with locoregional PCa	No ADT	GnRH agonist and/or AA	CHD MI SCD	1.16 (1.10–1.21) 1.11 (1.01–1.21) 1.16 (1.05–1.27)
Tsai et al. [15]	US CaPSURE (1995–2004)	4,892 Men with localized PCa	No ADT	GnRH agonist and/or AA	CV mortality with RP CV mortality with EBRT, BT or CT	2.6 (1.4–1.7) 1.2 (0.8–1.9)
Saigal et al. [16]	SEER (1992–1996)	22,816 Men with PCa	No ADT	Any medical ADT	CV morbidity	1.20 (1.15–1.26)
Alibhai et al. [19]	Ontario Cancer Registry (1995–2005)	19,079 Men with PCa	No ADT	GnRH agonist and/or AA Orchiectomy	AMI SCD Diabetes	0.92 (0.84–1.00) 0.96 (0.83–1.10) 1.24 (1.15–1.35)
Keating et al. [6]	US VHA (2001–2004)	37,443 Men with locoregional PCa	WW/AS	GnRH agonists, orchiectomy, AA, combined androgen blockade	CHD MI SCD Stroke	1.17 (1.06–1.39) 1.21 (1.01–1.44) 1.28 (1.05–1.57) 1.18 (1.02–1.36)
Van Hemelrijck et al. [7]	PcBaSE Sweden (1997–2007)	76,601 Men with PCa	RP, WW/AS	GnRH agonist AA GnRH + AA Orchiectomy Medical or surgical ADT	IHD MI Heart failure Stroke	1.34 (1.25–1.43)[b] 1.47 (1.35–1.60)[b] 1.67 (1.54–1.80)[b] 1.27 (1.17–1.38)[b]
Hu et al. [17]	SEER (1992–2007)	182,757 Men with locoregional PCa	No ADT	GnRH agonist Orchiectomy	PAD VTE	1.15 (1.11–1.19) 1.10 (1.04–1.16)
Jespersen et al. [10]	Danish Cancer Registry (2002–2010)	31,571 Men with PCa	No ADT	GnRH agonist/AA Orchiectomy	MI Stroke	1.31 (1.16–1.49) 1.19 (1.06–1.35)
Gandaglia et al. [18]	SEER (1995–2009)	140,474 Men with non-metastatic PCa	No ADT	GnRH agonist Orchiectomy	AMI CAD SCD	1.09 (1.04–1.15) 1.11 (1.07–1.15) 1.18 (1.12–1.24)

Tivesten et al, Urol Onc 2015

Rischio CV: summary

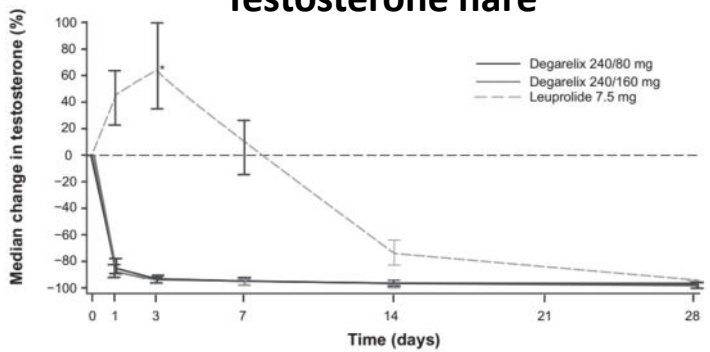
- **Molti degli studi osservazionali hanno mostrato un aumento degli eventi cardiovascolari non fatali**
- **L'associazione con la mortalità per eventi CV è ancora incerta**

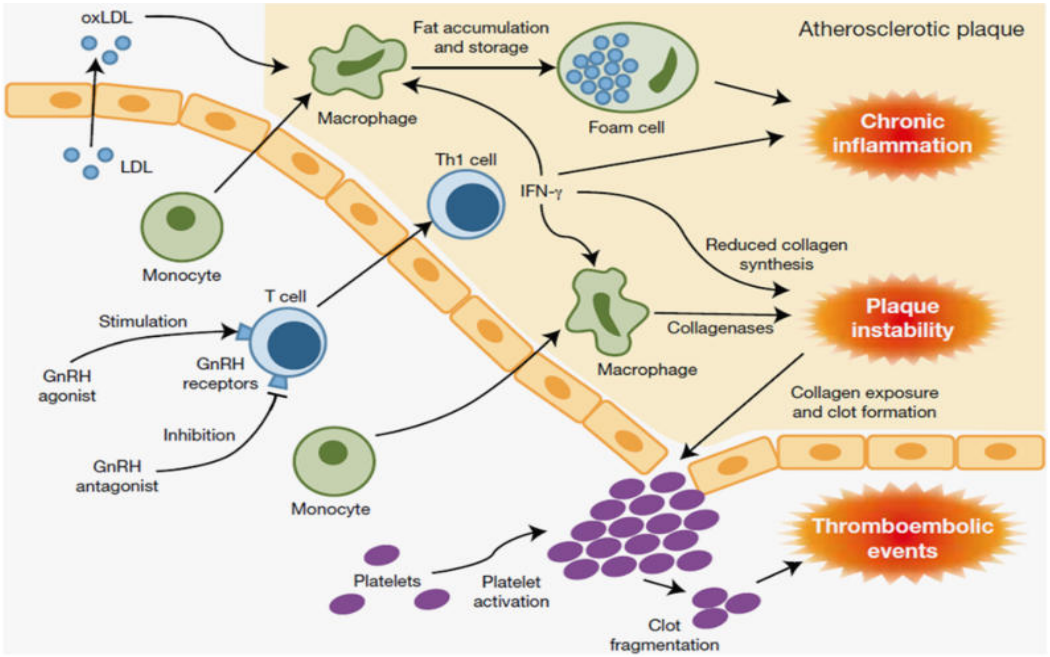
- **I pazienti più a rischio sembrano essere quelli:**
  - **> 65 anni**
  - **Pregressi eventi CV o con fattori di rischio per malattie CV**
  - **Trattati con GnRH analoghi**

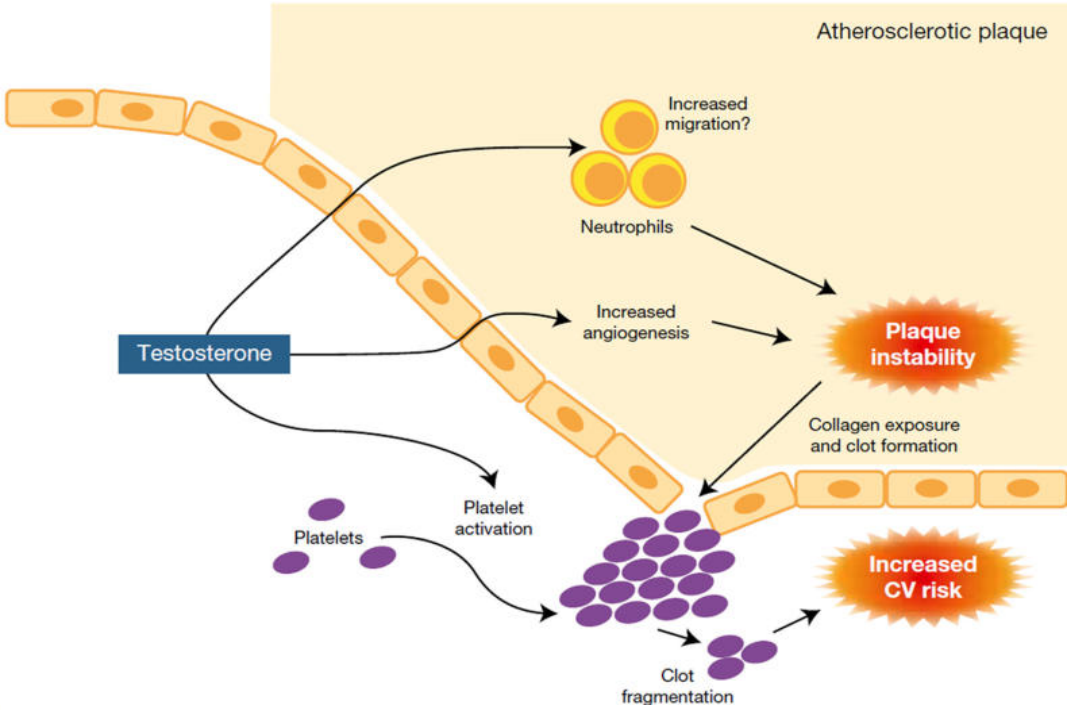
Tivesten et al, Urol Onc 2015

Rischio CV: meccanismi

Testosterone flare



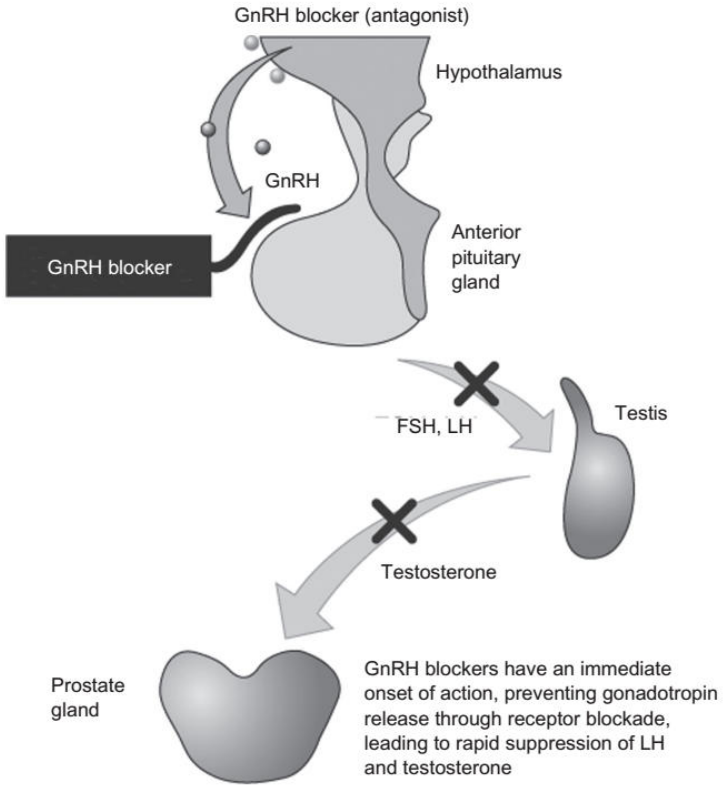


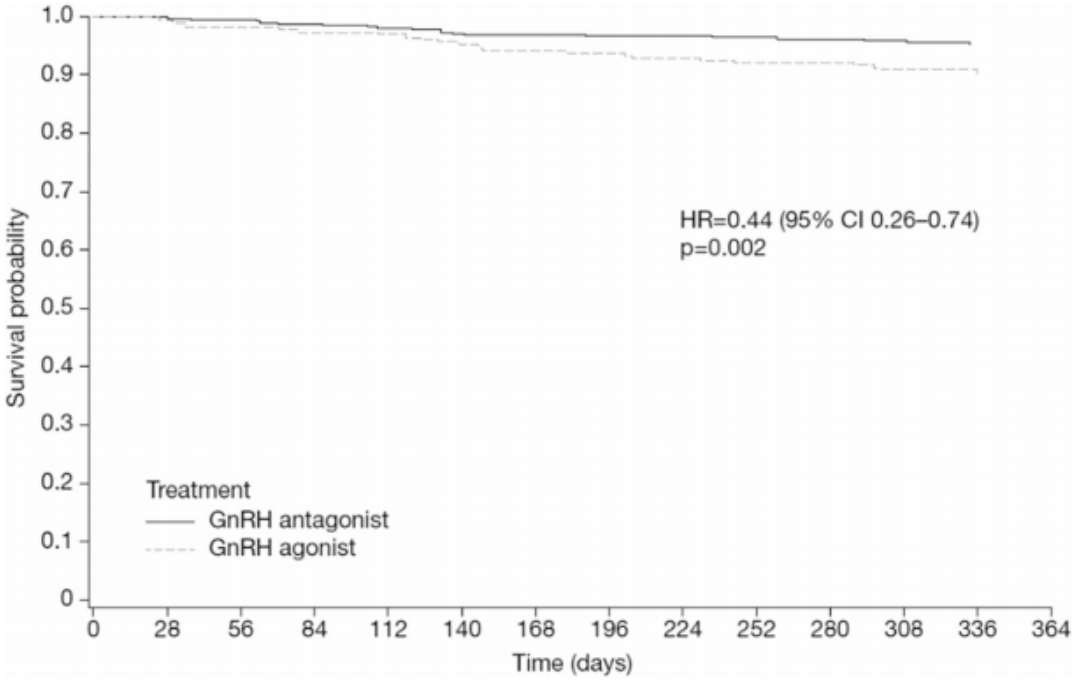


GnRHR, cellule immunitarie e destabilizzazione della placca

Tivesten et al, Urol Onc 2015

GnRH antagonisti e rischio CV



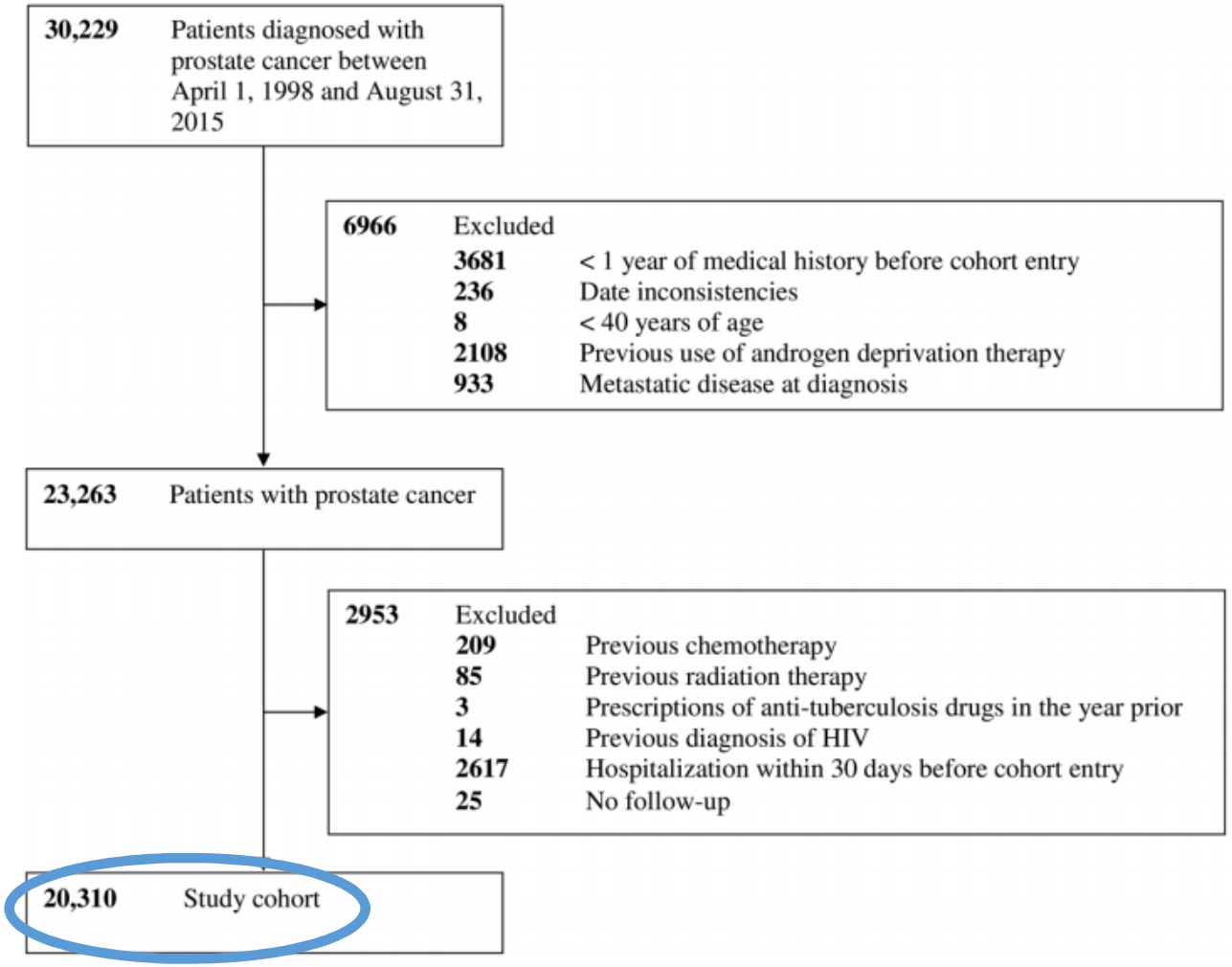


Van Poppel et al, CM&R 2010

ADT & polmonite acquisita in comunità (CAP)

Tipi di ADT:
- **GnRH analoghi**
- **Antiandrogeni orali**
- **Estrogeni**
- **Orchiectomia bilaterale**

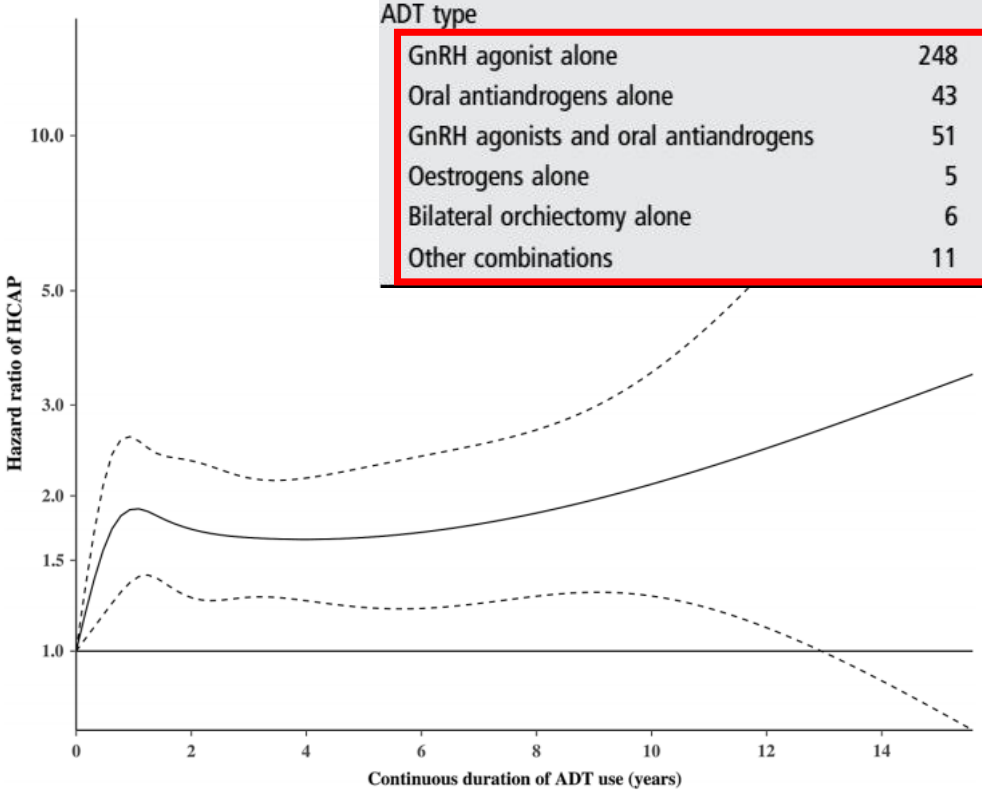
Follow-up: 4,3±3,4 anni



Hicks BM et al, Thorax 2017

ADT & CAP

Exposure to ADT	Events	Person- years	Incidence rate* (95% CI)	Crude HR	Adjusted HR (95% CI)†
Non-use	147	38 535	3.8 (3.2–4.5)	1.00	1.00 (reference)
Current use	364	30 052	12.1 (10.9–13.4)	3.32	1.81 (1.47–2.23)
Past use	110	17 713	6.2 (5.1–7.5)	1.44	1.23 (0.95–1.60)
Duration of current use, months					
<6	63	6506	9.7 (7.4–12.4)	2.62	1.73 (1.23–2.42)
6–12	45	5076	8.9 (6.5–11.9)	2.85	1.76 (1.19–2.60)
13–18	41	3610	11.4 (8.2–15.4)	4.29	2.45 (1.64–3.67)
19–24	30	2859	10.5 (7.1–15.0)	2.93	1.62 (1.02–2.56)
≥25	185	12 001	15.4 (13.3–17.8)	3.69	1.79 (1.39–2.30)
ADT type					
GnRH agonist alone	248	21 426	11.6 (10.2–13.1)	3.25	1.73 (1.39–2.16)
Oral antiandrogens alone	43	3874	11.1 (8.0–15.0)	2.93	1.64 (1.16–2.32)
GnRH agonists and oral antiandrogens	51	3575	14.3 (10.6–18.8)	3.66	2.18 (1.56–3.03)
Oestrogens alone	5	130	38.5 (12.5–89.8)	8.83	4.50 (1.82–11.17)
Bilateral orchiectomy alone	6	405	14.8 (5.4–32.2)	3.73	2.32 (1.02–5.30)
Other combinations	11	643	17.1 (8.5–30.6)	4.08	2.47 (1.33–4.61)



- **Aumento dell'81% del rischio di ospedalizzazione per CAP**
- **Indipendente dalla durata del trattamento**
- **Indipendente dal tipo di trattamento**

- **Pregresso uso di ADT non è associato ad aumento rischio**

Hicks BM et al, Thorax 2017

ADT & CAP: meccanismi

- **<u>Nell'uomo</u>:**
  - **Recettori per gli androgeni sono presenti sugli organi linfoidi primari (timo, midollo osseo) e stimolano la proliferazione dei precursori dei granulociti e la produzione di neutrofili**
  - **ADT potrebbe compromettere la risposta immunitaria interferendo con la funzione delle cellule T**

- **<u>Nei ratti</u>, ADT determina:**
  - **alterazioni morfologiche e biochimiche delle cellule polmonari**
  - **Alterazione della sintesi e secrezione di fosfolipidi nel surfattante polmonare**

ADT & insufficienza renale acuta

Table 4. Risk of Acute Kidney Injury Associated With Androgen Deprivation Therapy According to Type of Therapy

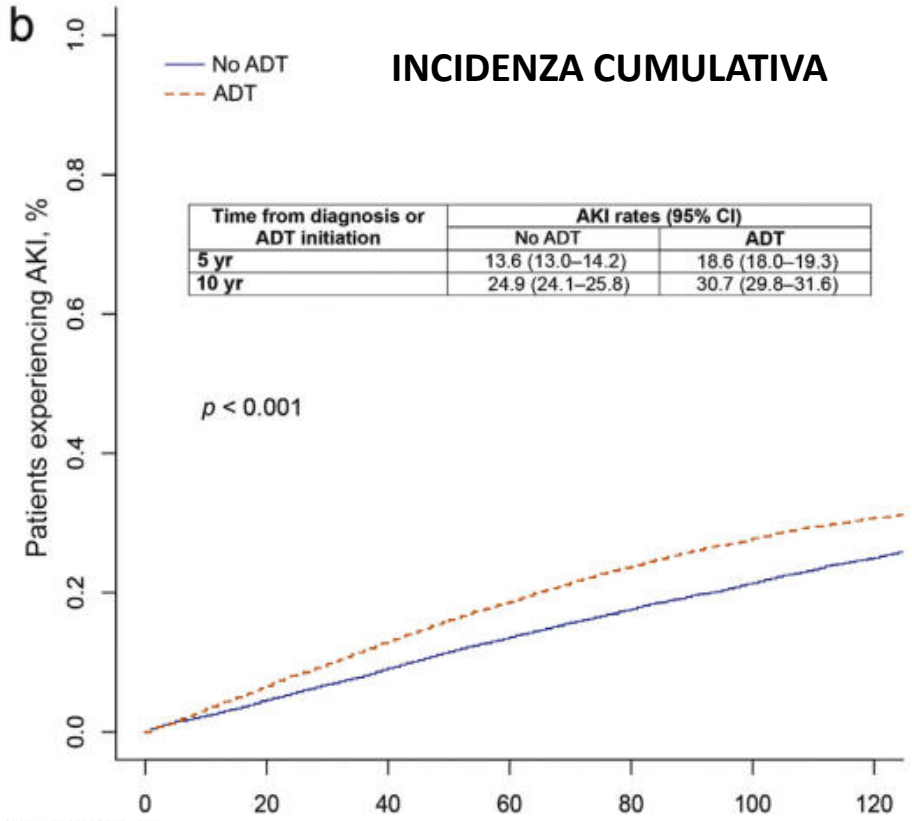
Exposure to Androgen Deprivation Therapy	No. (%)		OR (95% CI)	
	Cases (n = 232)	Controls (n = 2721)	Crude	Adjusted[a]
Never	40 (17.2)	842 (30.9)	1 [Reference]	1 [Reference]
Current[b]				
Combined androgen blockade	43 (18.5)	208 (7.6)	4.51 (2.80-7.27)	4.50 (2.61-7.78)
Estrogen only	5 (2.2)	15 (0.6)	7.03 (2.35-21.04)	4.00 (1.06-15.03)
Other combination therapies	19 (8.2)	69 (2.5)	5.56 (2.97-10.38)	4.04 (1.88-8.69)
Oral antiandrogens only	10 (4.3)	112 (4.1)	2.03 (0.97-4.23)	2.18 (0.95-5.01)
GnRH agonists only	85 (36.6)	949 (34.9)	1.99 (1.32-3.00)	1.93 (1.20-3.10)
Bilateral orchiectomy	6 (2.6)	67 (2.5)	1.59 (0.61-4.11)	1.84 (0.64-5.28)

Lapi F et al, JAMA 2013

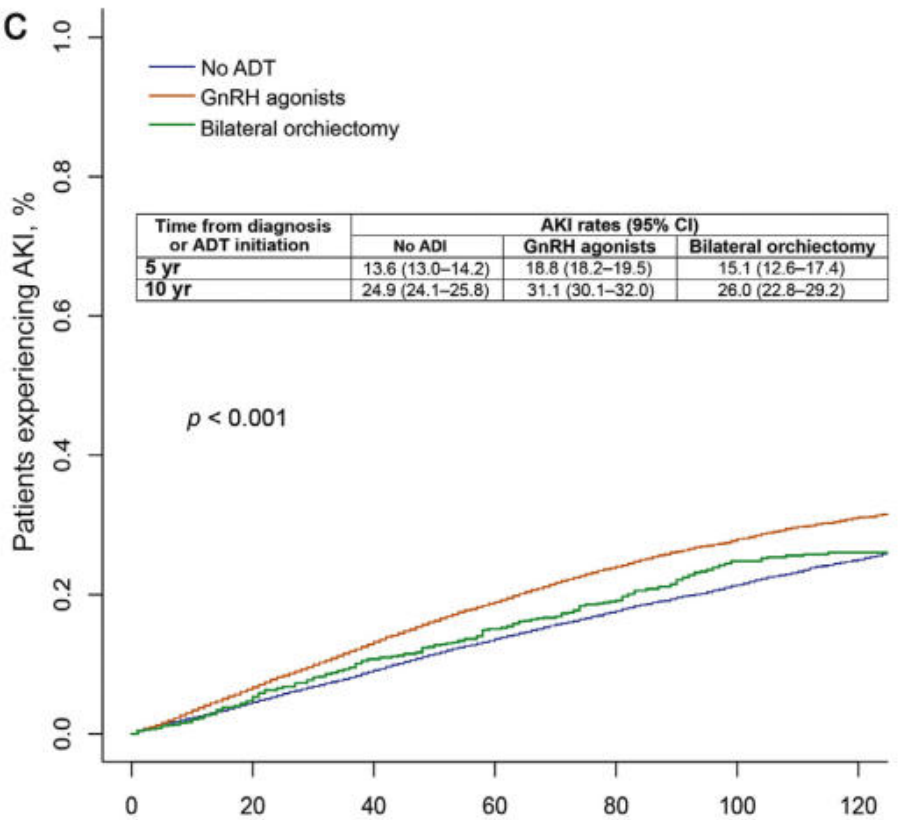
ADT & AKI

Gandaglia G et al, Eur Urol 2014

69292 pazienti (USA) con PC non M, >66 anni: ADT (GnRH analogo o orchiectomia) vs non ADT, follow-up medio: 7,1 anni.



Time from diagnosis or ADT initiation	AKI rates (95% CI)	
	No ADT	ADT
5 yr	13.6 (13.0–14.2)	18.6 (18.0–19.3)
10 yr	24.9 (24.1–25.8)	30.7 (29.8–31.6)



Time from diagnosis or ADT initiation	AKI rates (95% CI)		
	No ADI	GnRH agonists	Bilateral orchiectomy
5 yr	13.6 (13.0–14.2)	18.8 (18.2–19.5)	15.1 (12.6–17.4)
10 yr	24.9 (24.1–25.8)	31.1 (30.1–32.0)	26.0 (22.8–29.2)

Type of ADT				
No ADT	1 (ref.)		1 (ref.)	
GnRH agonist	1.28 (1.22–1.34)	<0.001	1.24 (1.18–1.31)	<0.001
Bilateral orchiectomy	0.93 (0.81–1.08)	0.4	1.11 (0.96–1.29)	0.1

NNH: esposizione di 20 e 17 pz a ADT risulta in una diagnosi di AKI a 5 e 10 anni, rispettivamente

ADT & AKI: meccanismi

1. **<u>Indiretto</u>: ↓ testosterone: dislipidemia, DM, massa grassa → effetti negativi sul filtrato glomerulare**
2. **<u>Diretto</u>: testosterone potrebbe proteggere la funzione renale inducendo vasodilatazione a livello regionale**

MA

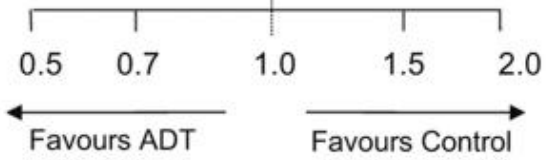
Orchiectomia non è associata ad AKI

→ Effetto di classe? Eventi ischemici secondari all'effetto negativo sulle placche aterosclerotiche?

ADT & stroke

6 studi, 160485 pazienti

Sub groups	ADT event/non-event	Control event/non-event	Hazard Ratio (95%CI)	P	P_{trend}
Types of ADT					**< 0.001**
AA	369/4709	2739/44570	1.06 (0.71, 1.57)	0.78	
GnRH	11669/37623	2739/44570	1.20 (1.12, 1.28)	**< 0.001**	
GnRH+AA	1757/12149	2739/44570	1.23 (1.13, 1.34)	**< 0.001**	
Orchiectomy	795/7168	3661/63955	1.37 (1.33, 1.64)	**0.001**	
Overall	5578/74538	5134/85947	1.12 (0.95, 1.32)	0.16	

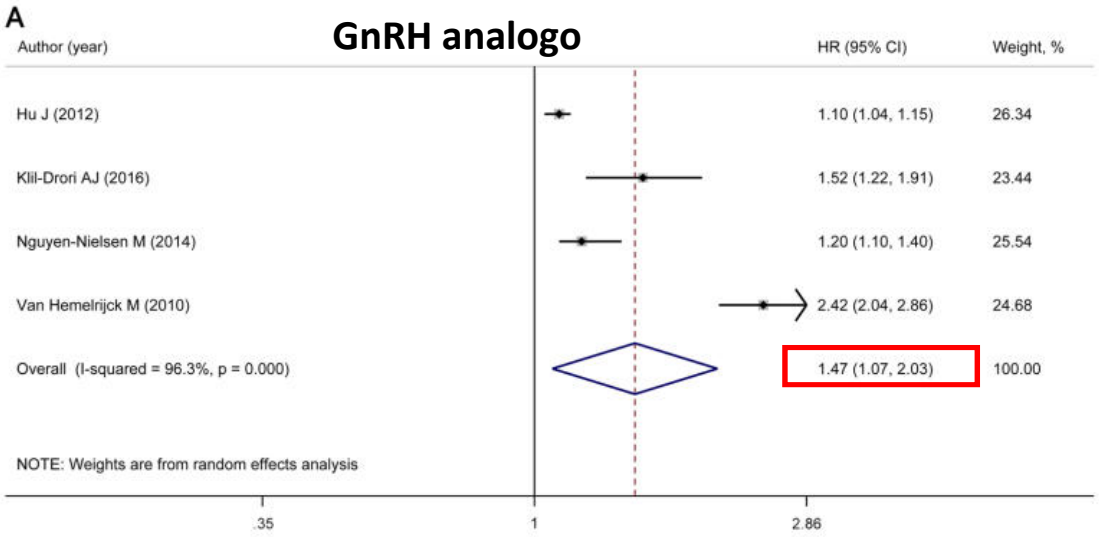


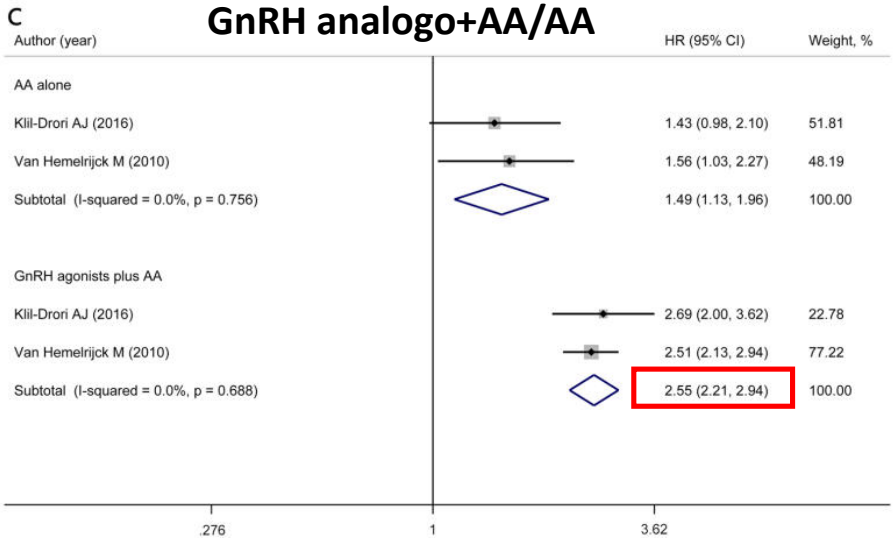
→ Tendenza ad aumentato rischio di stroke

Meng F et al, BMC Cancer 2016

ADT & TVP

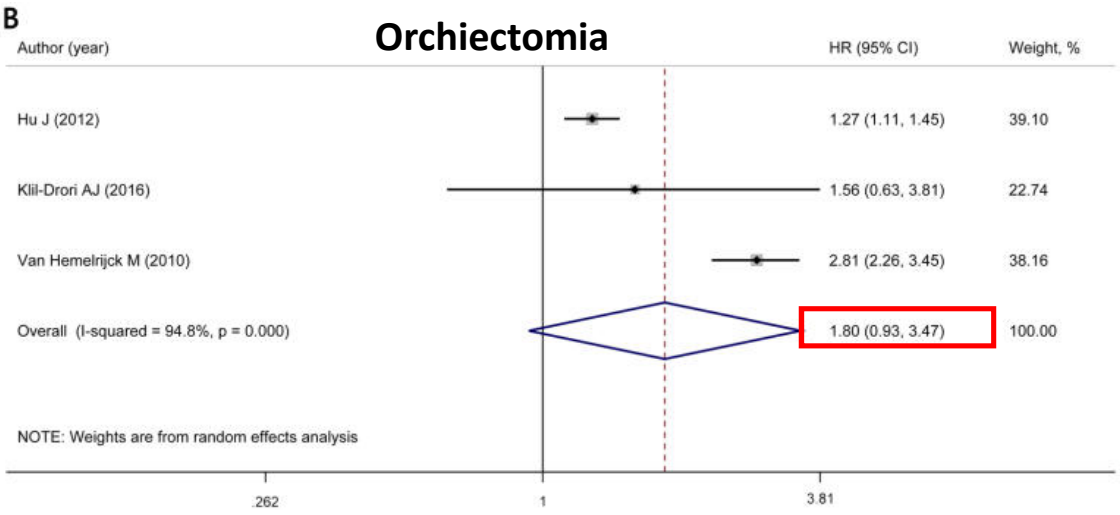
Guo Z et al, PC&PD 2018





TVP associata ad uso di:

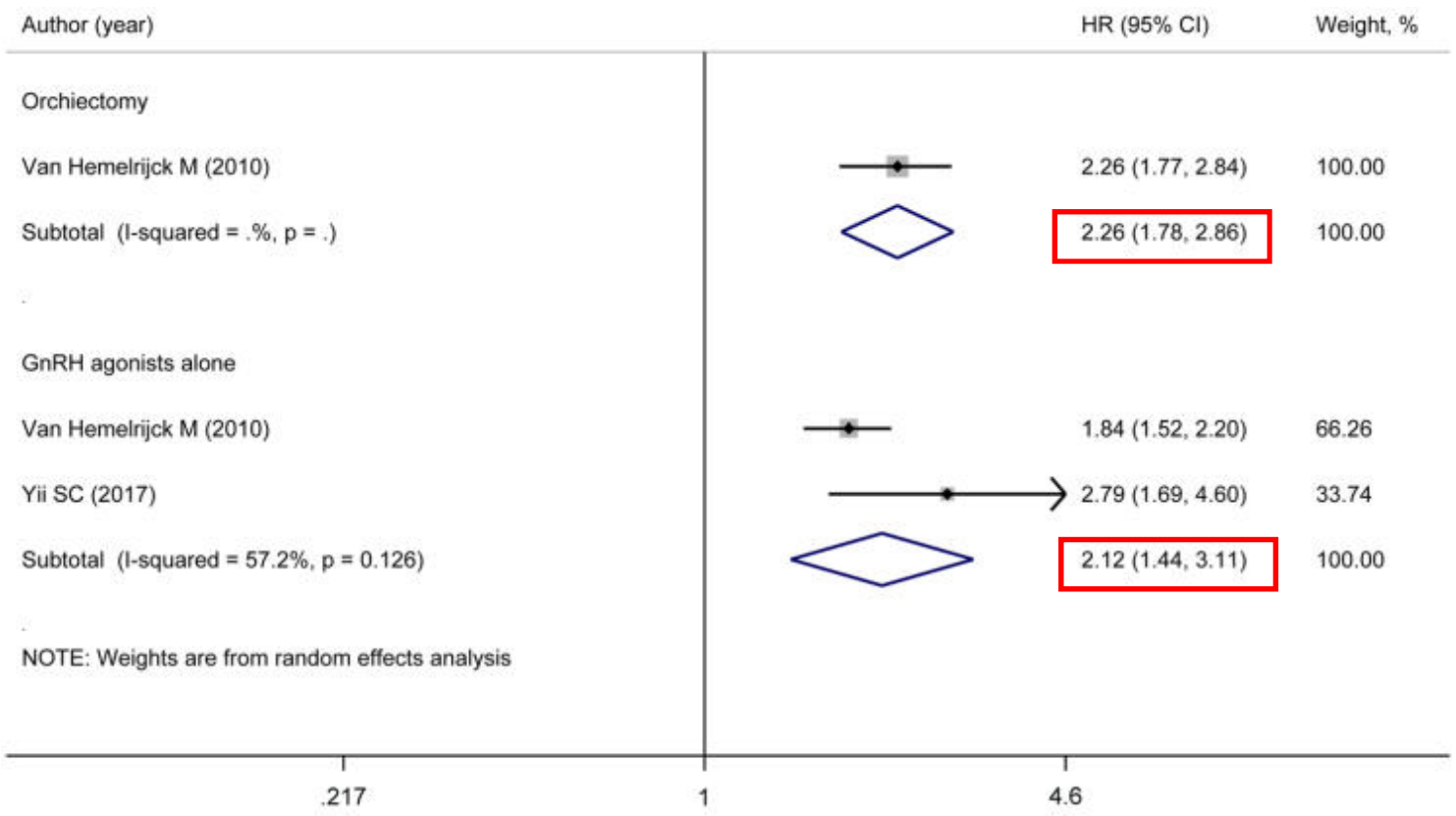
- **GnRH analogo**
- **Antiandrogeni**
- **GnRH + AA**



ADT & embolia polmonare

EP associata a:

- **GnRH analogo**
- **Orchiectomia**



Guo Z et al, PC&PD 2018

CONCLUSIONI

- **La deprivazione androgenica si accompagna a numerosi possibili effetti avversi in particolare a livello sessuale, metabolico, cardiovascolare, tromboembolico**

PREVENIRE E MITIGARE

1. **RAPPORTO RISCHIO/BENEFICIO → ACCURATA SELEZIONE DEI PZ**
2. **VALUTAZIONE MULTIDISCIPLINARE (endocrinologo/diabetologo, urologo, psicologo, cardiologo, pneumologo, nefrologo…): messa in atto di strategie (stile di vita, farmacoterapia) per migliorare la QoL e ridurre i fattori di rischio cardio-metabolici e quindi la morbidità e la mortalità**