



# Tumori ipofisari clinicamente non funzionanti



ITALIAN CHAPTER

Roma, 8-11 novembre 2018



[www.assoziazionemediclandocrologi.it](http://www.assoziazionemediclandocrologi.it)

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## 17° Congresso Nazionale AME

Joint Meeting with AAACE Italian Chapter

### Update in Endocrinologia Clinica

8-11 novembre 2018

Roma

PROGRAMMA DEFINITIVO



## Terapie complementari: quali, a chi e quando ?

Pietro Maffei

Clinica Medica 3 – DIMED

Azienda Ospedaliera Padova

*Sabato 10 novembre 2018 – Ergife Palace Hotel*



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# Background terapia con SSA



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- ✓ Espressione SSTR3 > SSTR2 nei NFPA (Taboada et al. 2007)
- ✓ Espressione SSTR5 > SSTR2 nei NFPA (Fusco et al. 2012)
- ✓ La somatostatina nativa e analoghi selettivi di SSTR3 o SSTR2 inibiscono la subunità alfa (Pawlikowski et al. 2007)



# Medical therapy for clinically non-functioning pituitary adenomas



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Authors (year of publication)	Visual field			Tumour volume			Octreotide	
	Improved	Unchanged	Worsened	Increased	Unchanged	Decreased	Dose ( $\mu\text{g/d}$ )	Duration (months)
Warnet <i>et al.</i> (1989)	3/5	2/5	0/5	0/2	2/2	0/2	100–300	1–12
Turpin <i>et al.</i> (1991)				0/1	1/1	0/1	300–450	6
De Bruin <i>et al.</i> (1992)	3/4	1/4	0/4	0/4	4/4	0/4	1200	3–6
Katznelson <i>et al.</i> (1992)	1/3	2/3	0/3				200–750	2
Gasperi <i>et al.</i> (1993)	1/5	3/5	1/5	2/8	6/8	0/8	300	3–6
Merola <i>et al.</i> (1993)	1/9	8/9	0/9	0/19	18/19	1/19	150–300	1–12
Plockinger <i>et al.</i> (1994)				2/14	12/14	0/14	300–1500	3
Liuzzi <i>et al.</i> (1991)	1/20	19/20	0/20	3/20	14/20	3/20	300–500	3–12
Warnet <i>et al.</i> (1997)	9/22	9/22	4/22	3/7	3/7	1/7	300–600	2
Borson-Chazot <i>et al.</i> (1997)	8/16	6/16	2/16	0/16	16/16	0/16	300	1
Colao <i>et al.</i> (1999)				2/9	7/9	0/9	300–600	12
<b>Summary</b>	<b>27/84</b>	<b>50/84</b>	<b>7/84</b>	<b>12/100</b>	<b>83/100</b>	<b>5/100</b>		



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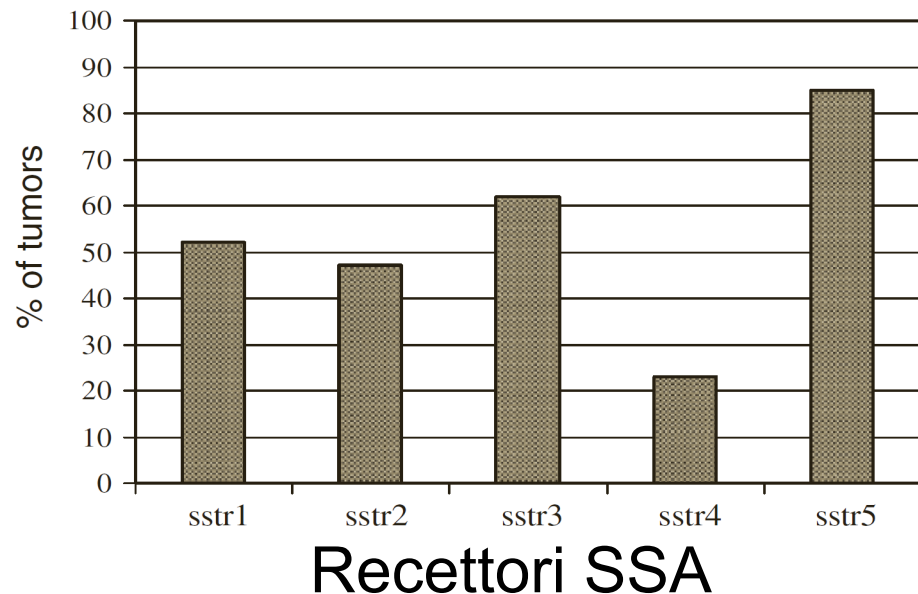
# Treatment with octreotide LAR in clinically non-functioning pituitary adenoma: results from a case-control study



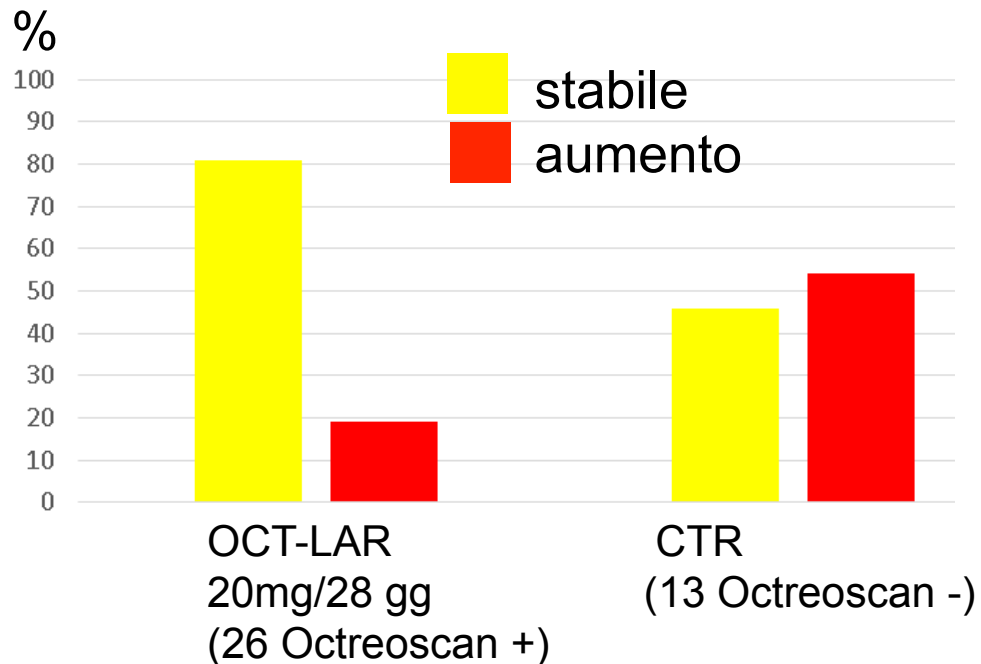
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## Trattamento o CTR per 37 mesi



Recettori SSA



modificata da Fusco et al, Pituitary 2012



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# Razionale terapia con DA



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- ✓ I NFPT esprimono recettori D2R:
  - > nei gonadotropi e null-cell NFPT
  - > vs GHomi
  - < vs ipofisi normale o prolattinomi
- ✓ I DA riducono la secrezione di gonadotropine



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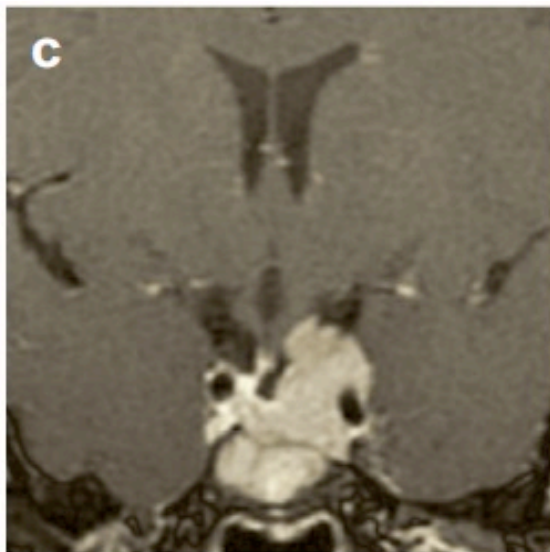
# Terapia con Cabergolina



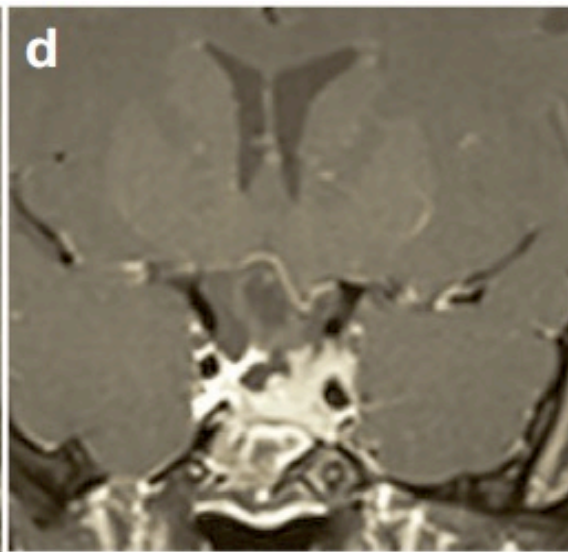
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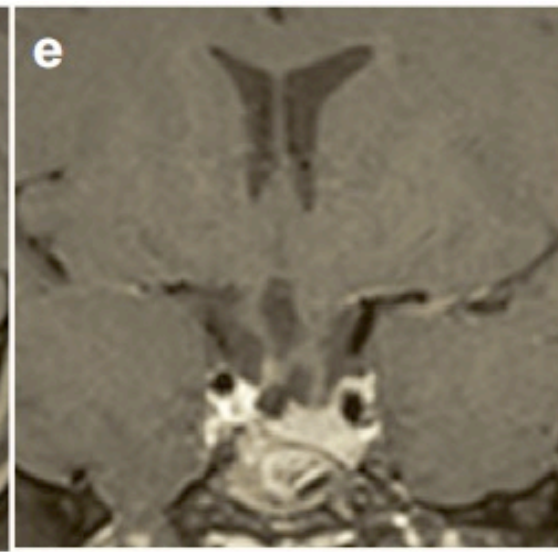
**Titolazione CAB: 0.5 mg/sett → max 2-3 mg/sett**



November 2013



November 2015



February 2017

Cooper & Greeman, Frontiers in Endocrinology 2018

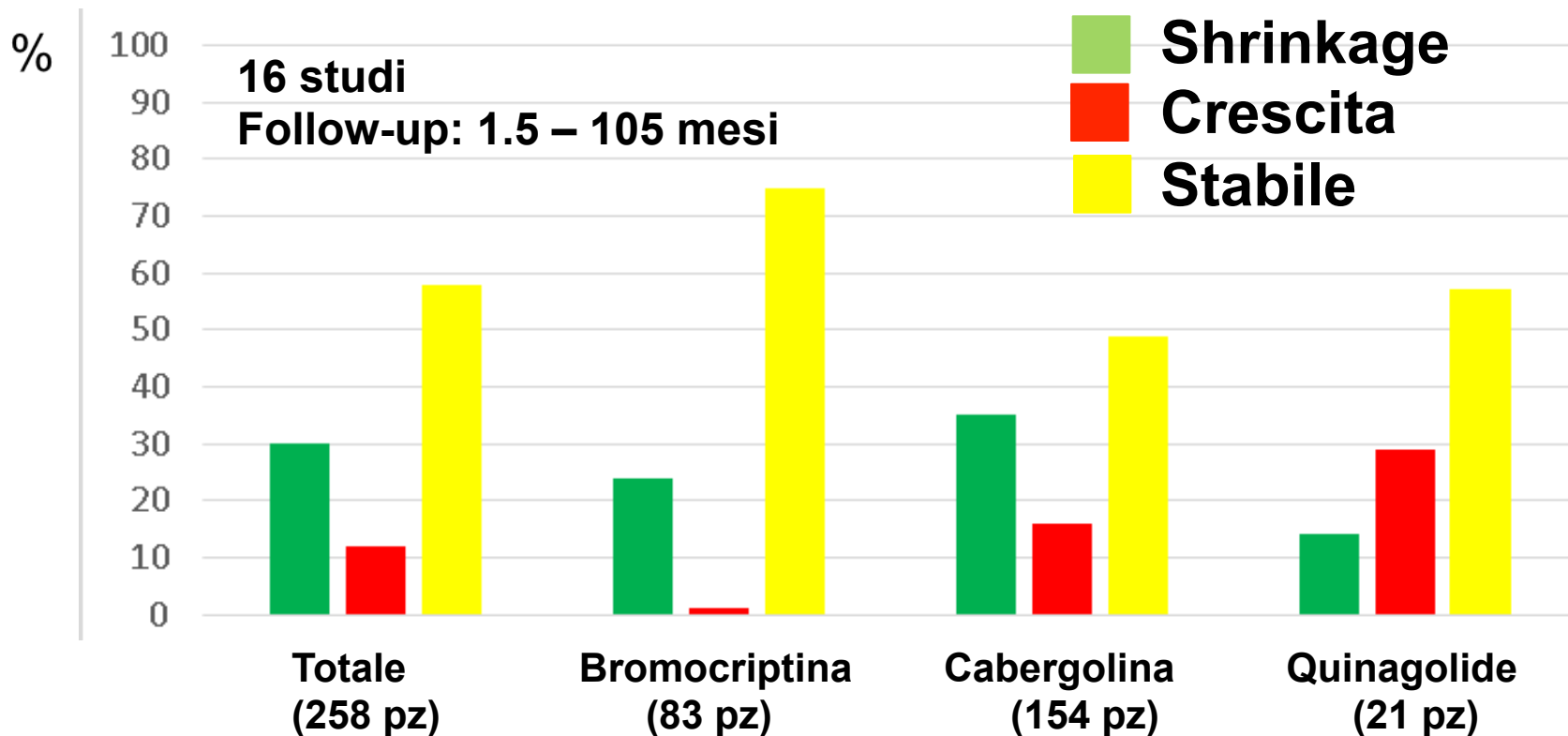


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# Terapia con DA nei NFPA



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modificata da Cooper & Greeman, Frontiers in Endocrinology 2018

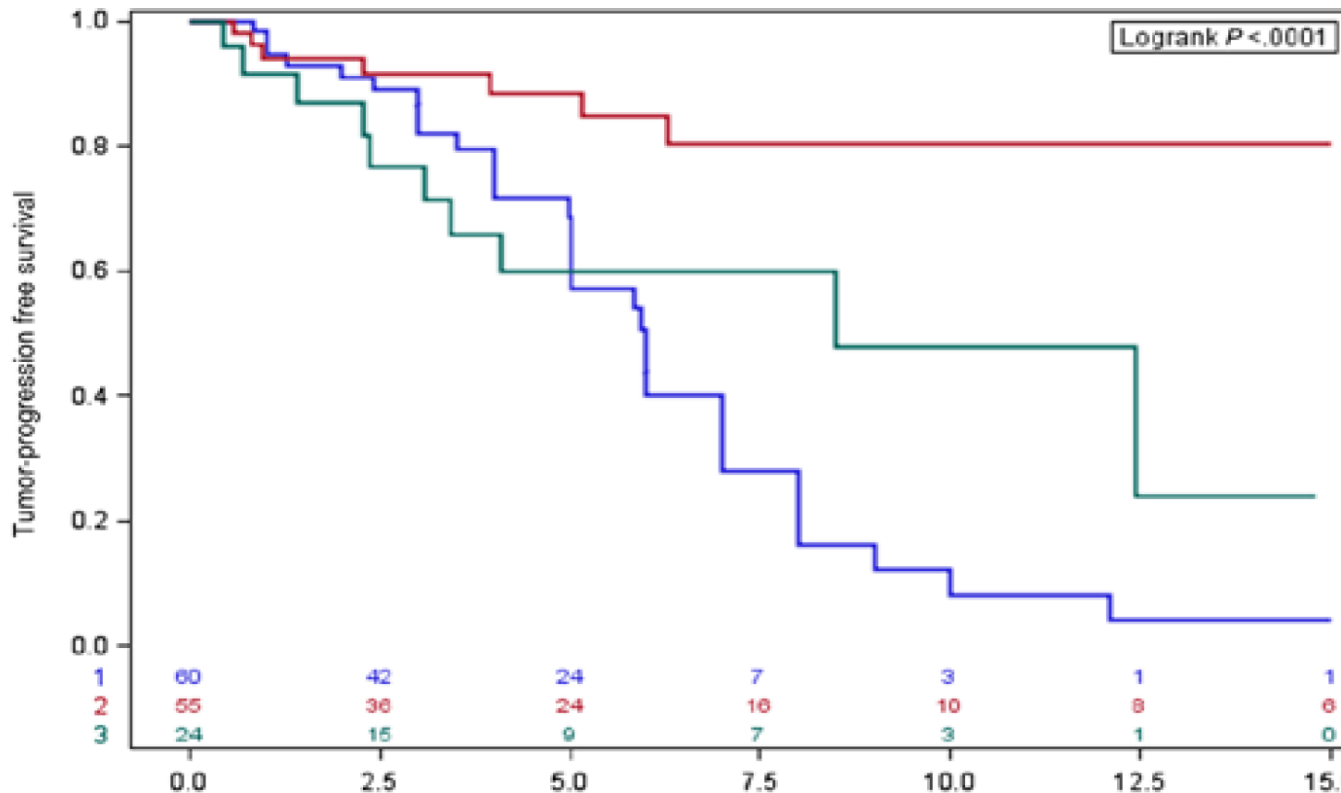


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# Treatment of clinically nonfunctioning pituitary adenomas with dopamine agonists



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DA post NCH

**BCT: 2.5-10 mg/die**  
**CAB: 0.5-3.5 mg/sett**

DA alla recidiva

NO terapia

anni

Greenman et al, EJE 2016

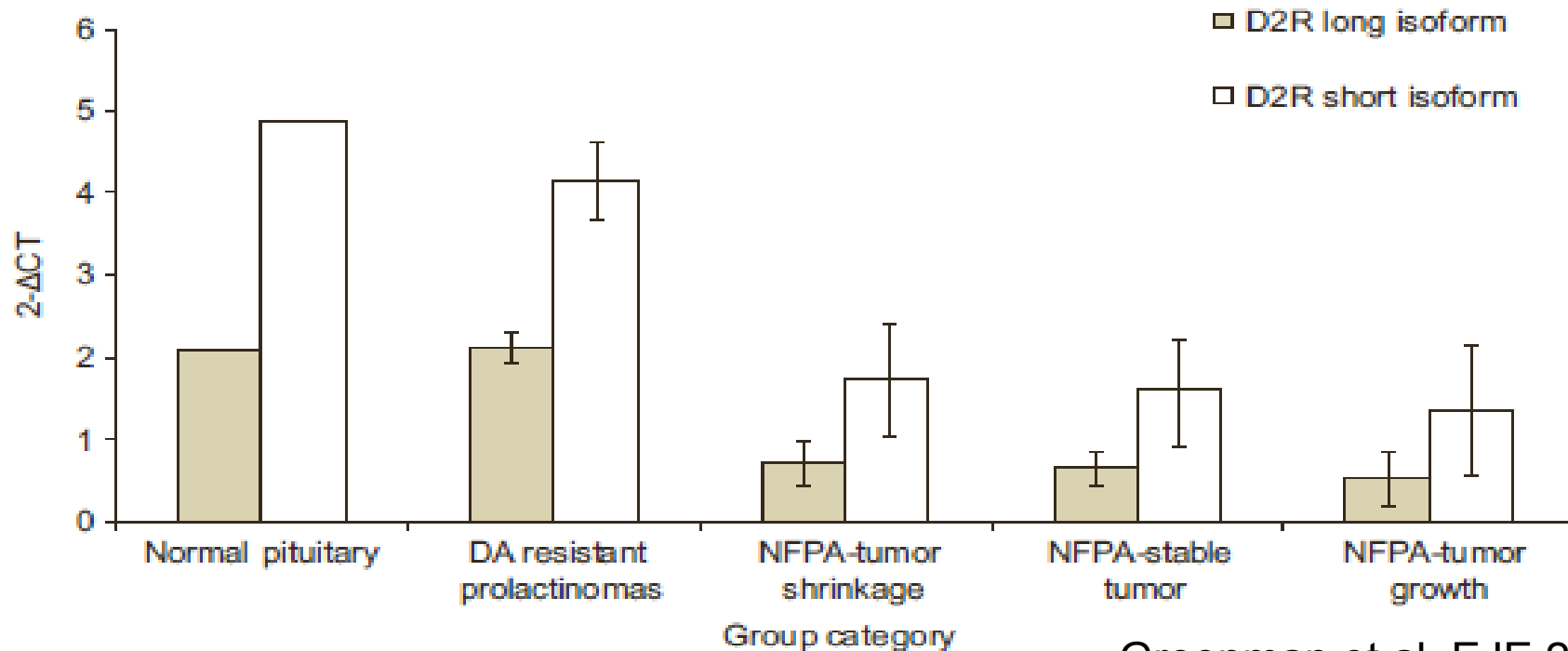




# Treatment of clinically nonfunctioning pituitary adenomas with dopamine agonists



## Nessuna relazione fra risposta e recettori o isoforme D2R





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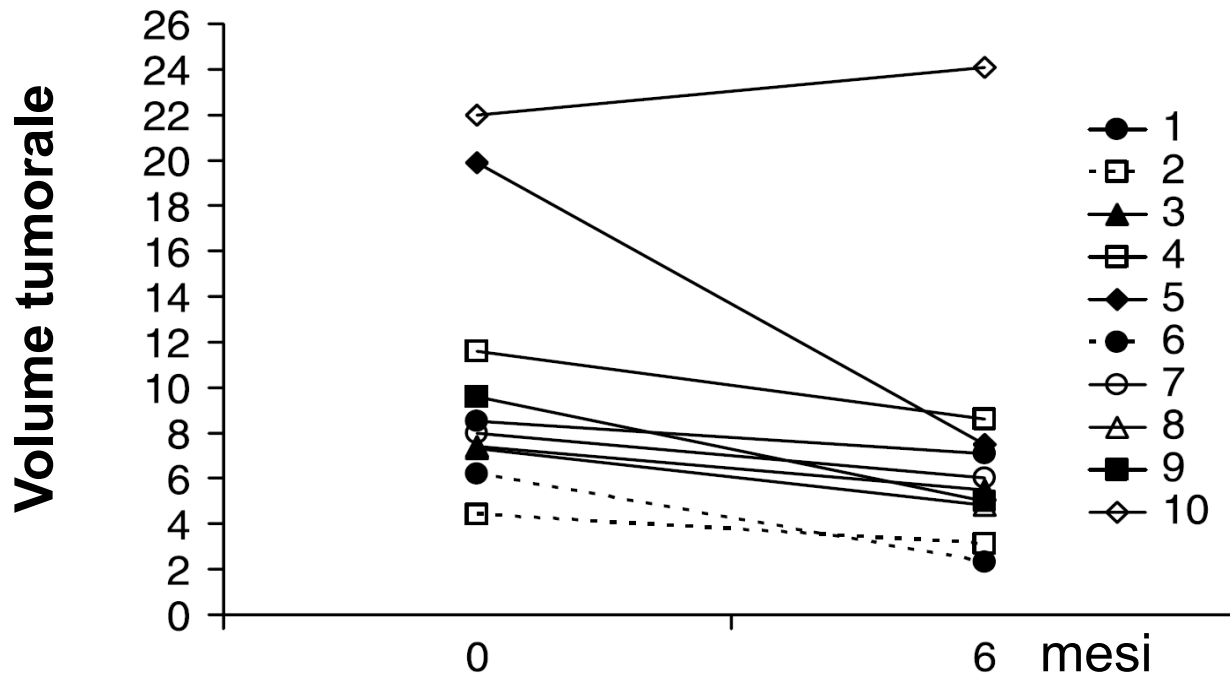
# Terapia combinata



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## Lanreotide 60/14 gg + CAB 0.5 mg/die alterni



Colao et al. Endocrine 2003



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# Treatment of aggressive pituitary tumours and carcinomas: results of a European Society of Endocrinology (ESE) survey 2016



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**Table 1** Baseline characteristics stratified by diagnosis. Data are presented as *n* (%)

	Aggressive pituitary tumour	Pituitary carcinoma	P-Value
Total ( <i>n</i> )	125	40	
Age at diagnosis, mean (s.d.)	42.7 (16.2)	44.7 (15.1)	0.51
Gender ( <i>n</i> = 164)			0.82
Female ( <i>n</i> = 59)	44 (35.5%)	15 (37.5%)	
Male ( <i>n</i> = 105)	80 (64.5%)	25 (62.5%)	
Clinical subtype ( <i>n</i> = 165)			0.018
Clinically functioning ( <i>n</i> = 97)	72 (57.6%)	25 (62.5%)	
Initially silent becoming functional ( <i>n</i> = 17)	9 (7.2%)	8 (20.0%)	
Clinically non-functioning ( <i>n</i> = 51)	44 (35.2%)	7 (17.5%)	



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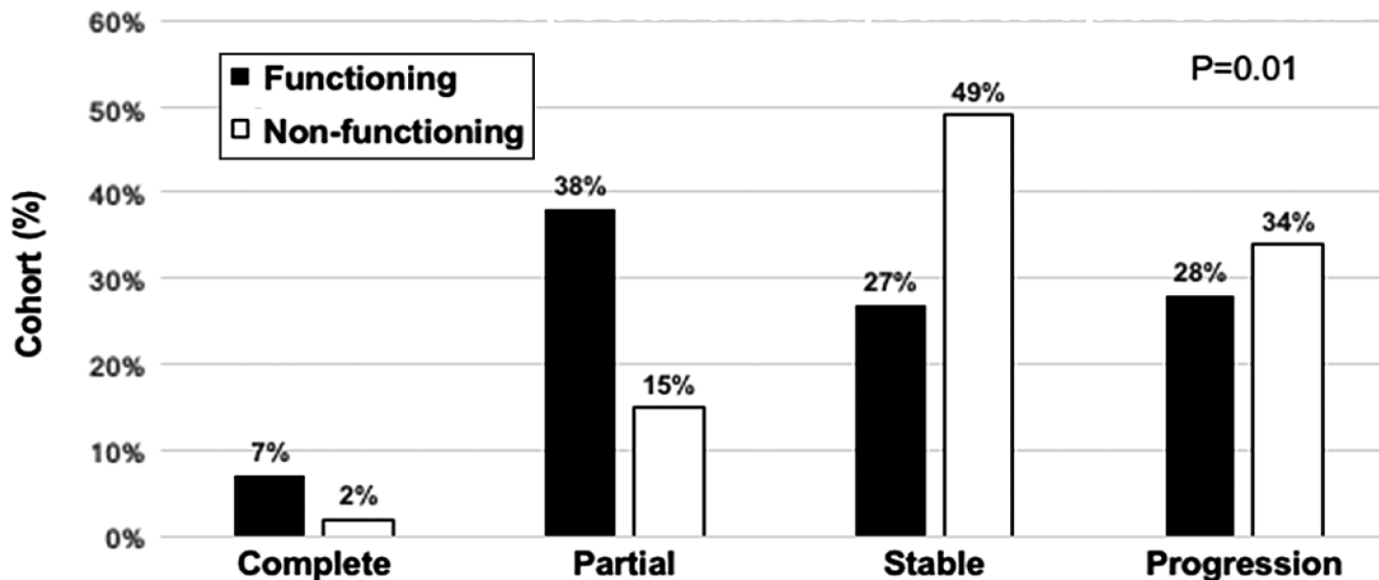
# Treatment of aggressive pituitary tumours and carcinomas: results of a European Society of Endocrinology (ESE) survey 2016



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## Risposta radiologica a terapia con TMZ



Response defined as complete=no visible tumour; partial response=30–99% regression, stable <30% regression and <10% progression, progression=>10% progression.

McCormack et al, EJE 2016

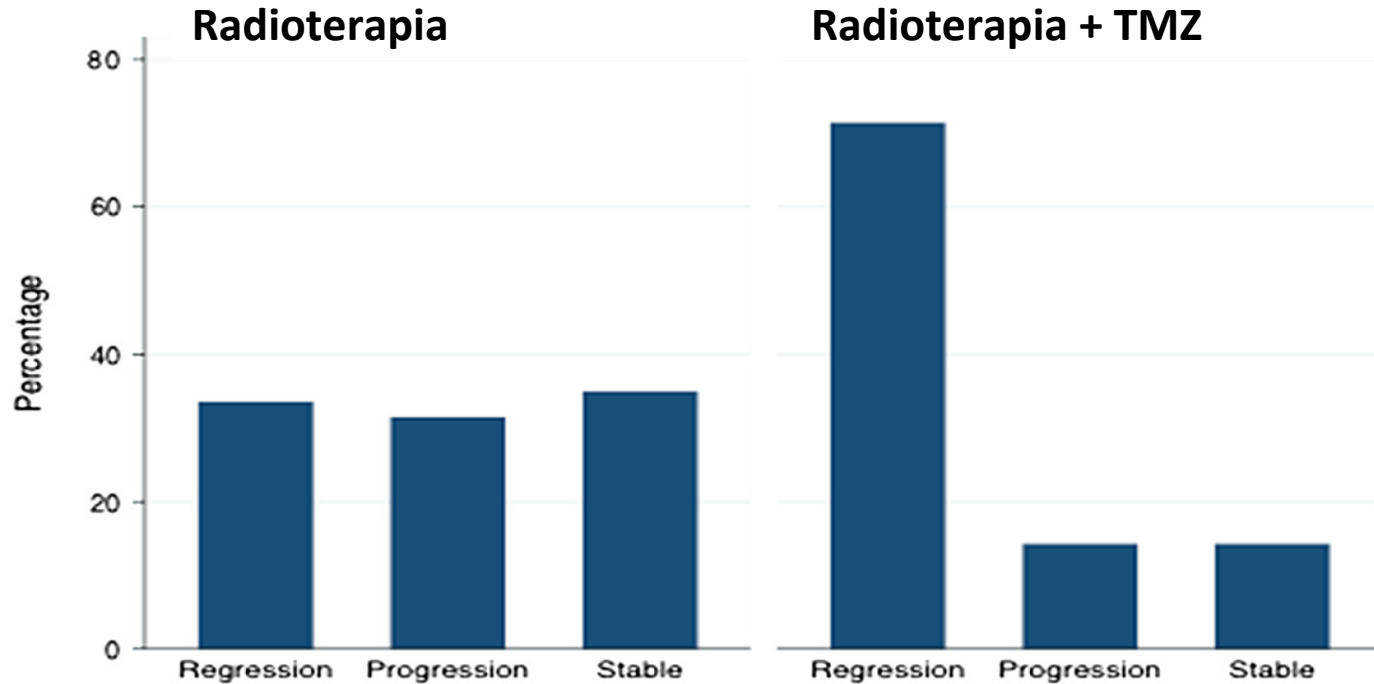


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# Treatment of aggressive pituitary tumours and carcinomas: results of a European Society of Endocrinology (ESE) survey 2016



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McCormack et al, EJE 2016

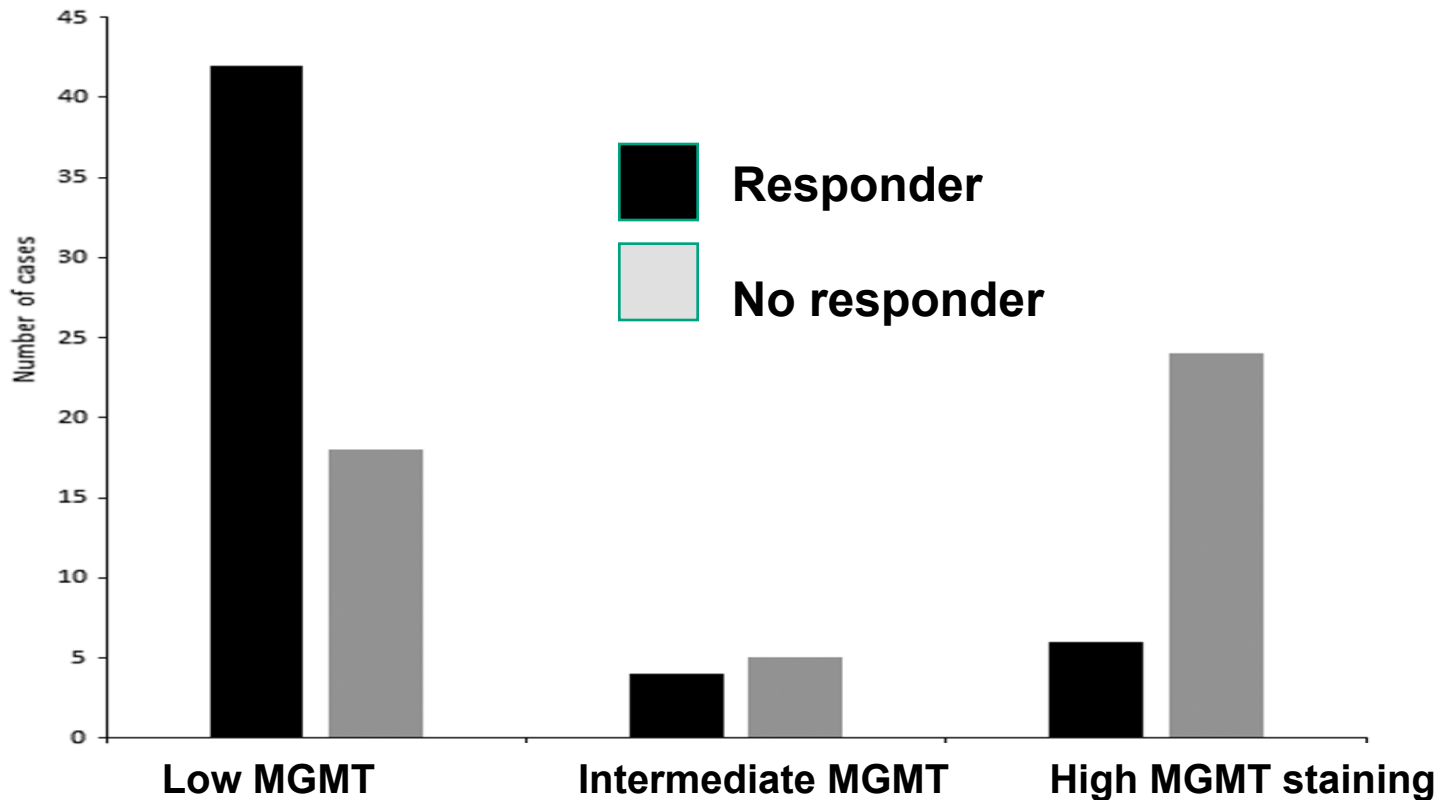


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# European Society of Endocrinology Clinical Practice Guidelines for the management of aggressive pituitary tumours and carcinomas



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Raverot et al. EJE 2018



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# European Society of Endocrinology Clinical Practice Guidelines for the management of aggressive pituitary tumours and carcinomas



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- ✓ TMZ in monoterapia first-line se crescita documentata: 150-200 mg/m<sup>2</sup> x 5 gg ogni 28 gg x 3 cicli (proseguire se risposta o ripetere in caso di recidiva)
- ✓ Rivalutazione radiologica dopo 3 cicli
- ✓ STOP TMZ se progressione radiologica
- ✓ Se rapida crescita, considerare RT + TMZ o altre CT
- ✓ Basso MGMT → maggiore risposta TMZ (ma esistono eccezioni)



# Peptide receptor radionuclide therapy in a patient with disabling non-functioning pituitary adenoma

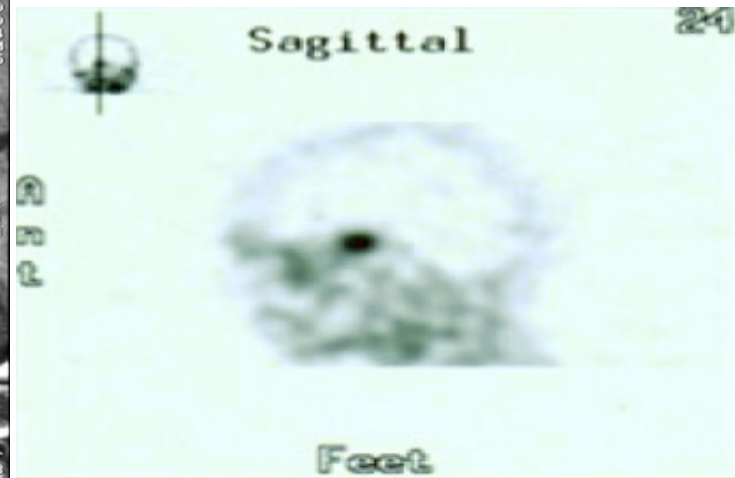


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## Lutezio-DOTATOC

## Octreoscan +



Komor et al. Pituitary 2014





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# <https://clinicaltrials.gov>



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- ✓ «Evaluate the efficacy and safety of Pasireotide LAR on the treatment of patients with clinically non-functioning pituitary adenoma» (Passion I)
  - Fase 2, completato; 24 settimane di terapia; 20 pazienti (Brasile)
- ✓ «Response to Cabergoline and Pasireotide in non-functioning pituitary adenoma and resistant prolactinoma»
  - Fase 2; in corso; PASI 900 mcg x 2 die vs CAB 3 mg/sett x 6 mesi; 21 pazienti arruolati (Brasile)
- ✓ «Dopamine D2 receptors (D2R) imaging in non-functioning pituitary adenoma (NFPA)»
  - Fase 3; deve iniziare; D2R positivi → terapia con CAB 2mg/sett o BCT 7.5 mg/die (Cina)
- ✓ «Pasireotide LAR therapy of silent corticotroph pituitary adenoma» (PASSILCORT)
  - Fase 2; in corso; studio pilota su 10 pazienti; 12 mesi di terapia con Pasireotide LAR 40/mese → 60/mese sulla base livelli di POMC o risposta radiologica (USA)