Temozolomide treatment for pituitary aggressive tumors and pituitary carcinomas: initial results and long term follow-up of a cohort of 31 cases

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Members of the French Society of Endocrinology were surveyed regarding the clinical characteristics of pituitary tumors treated with TMZ.

Patient	Sex	Age at diagnosis (yrs)	Type	Tumor	Ki67 %	p53 %	Mitosis/10	Surgeries	Radiotherapy	Time from diagnosis to TMZ treatment (yrs)	Short term response
1	F	42	ACTH	Adenoma	0,5	0	1	3	2	8	Yes
2	F	51	ACTH	Adenoma	5	10	5	3	2	10	Yes
3	F	41	ACTH	Adenoma				1	1		Yes
4	F	53	ACTH	Adenoma	1			1	1	1	Yes
5	F	13	ACTH	Adenoma				1	1	12	Yes
6	M	28	ACTH	Adenoma	7	7	2	0	1	0,25	Yes
7	F	36	ACTH	Adenoma	15	8	2	2	1	14	Yes
8	M	50	ACTH	Adenoma	20	60	8	1	2	5	No
9	M	55	ACTH	Adenoma				2	1	5	No
10	F	25	ACTH	Adenoma	8	1	2	2	1	1	No
11	M	38	ACTH	Carcinoma	10	1	7	4	2	14	Yes
12	F	ND	ACTH	Carcinoma	30			1+meta	2	6	Yes
13	M	31	ACTH	Carcinoma	20	10	3	3	2	6	No
14	M	45	ACTH	Carcinoma	0	0	4	2	1+meta	11	No
15	M	62	ACTH	Carcinoma	10	30		1	0		No
16	M	36	ACTH	Carcinoma	34	4	3	2	2	2	No
17	F	61	PRL	Adenoma	23			0	1	0	Yes
18	M	76	PRL	Adenoma				0	1	4	Yes
19	M	75	PRL	Adenoma				0	0	3	Yes
22	M	40	PRL	Adenoma	12	10	3	3	1	14	No
23	M	32	PRL	Adenoma	2	0,5	5	2	2	18	No
24	M	18	PRL	Adenoma	25	20		3	1	11	No
20	M	31	PRL	Carcinoma				1	1	11	Yes
21	M	38	PRL	Carcinoma	13			4	2	4	Yes
25	M	54	PRL	Carcinoma	7	1	8	5	2	14	No
26	F	30	PRL	Carcinoma	30	10	4	4	2	17	No
27	M	44	PRL/GH	Adenoma	30		20	1	1	1	Yes
28	M	50	PRL/GH	Adenoma	30			1	1	3	Yes
29	M	46	GH	Adenoma	10	2	2	2	1	10	No
30	M	26	GH	Carcinoma	25		6	3	2	4	No
31	M	36	NFPA	Adenoma				1	1	1	Yes

31 patients from 17 centers were included.

Treatment :

Temozolomide was administered 150-200 mg/j 1 cycles = 5 days a month,

Association with radiotherapy STUPP n=5

Patients	31
Mean Age at diagnosis (yrs) n=30	42,1 +/- 14,9
Sex ratio F/M	10/21
Adenomas / Carcinomas	20 / 11
ACTH	16
PRL	10
GH	2
PRL/GH	2
NFPA	1
Mean Ki67 (%) n=24	15,3 +/- 10,9
Mean p53 (%) n=17	10,3 +/- 15,1
Mean number of mitosis (n/10HPF) n=17	5 +/- 4,4
Mean time before treatment (yrs) n=29	7,2 +/- 5,5
Mean duration of treatment (cycles) n=30	8,2 +/-5,3
Mean Follow-up after TMZ end (months) n=27	20,4 +/- 18
Mean time before relapse after TMZ end in case of response (months) n=9	17,8 +/- 20

Response Criteria :

Hormonal Response : At least 50% of decrease of hormonal rate without tumoral progression

Tumoral Response : At least 30% of decrease of the largest diameter without hormonal progression

No Response : Stability, progression or decrease under limits above.

Initial presentation and response to TMZ

	Response n=17 (54,8%)	No response n=14 (45,2%)	P value
ACTH n= 16	9 (56%)	7 (44%)	0,287*
PRL n=10	5 (50%)	5 (50%)	
PRL/GH n=2	2 (100%)	0	
NFPA n=1	1 (100%)	0	
GH n=2	0	2 (100%)	
Adenomas n=20	13 (65%)	7 (35%)	0,125*
Carcinomas n=11	4 (36%)	7 (64%)	
mean Ki67 % n=24	15	15,6	0,907**
Mean Mitosis n/10 HPF n=17	6,2	4,4	0,760**
Mean p53 % n=17	5,2	12,4	0,489**
Mean time between diagnosis and treatment (yr)	5,75	9,07	0,095**
Sex Ratio M=21/ F= 10	9/8	12/2	0,052*
Death n=10	2 (20%)	8 (80%)	0,007*

*Chi squared, **Wilcoxon

Tolerance

Temozolomide was **well tolered**. There were no withdraw due to treatment.

Side effects :

Thrombopenia n = 4, Pancytopenia n = 3,
Tiredness n = 5, Digestives disorders n= 5

Long term follow-up

1 (ACTH) complete remission 2 years after TMZ end.

2 partial remissions 1 and 3 years after TMZ end.

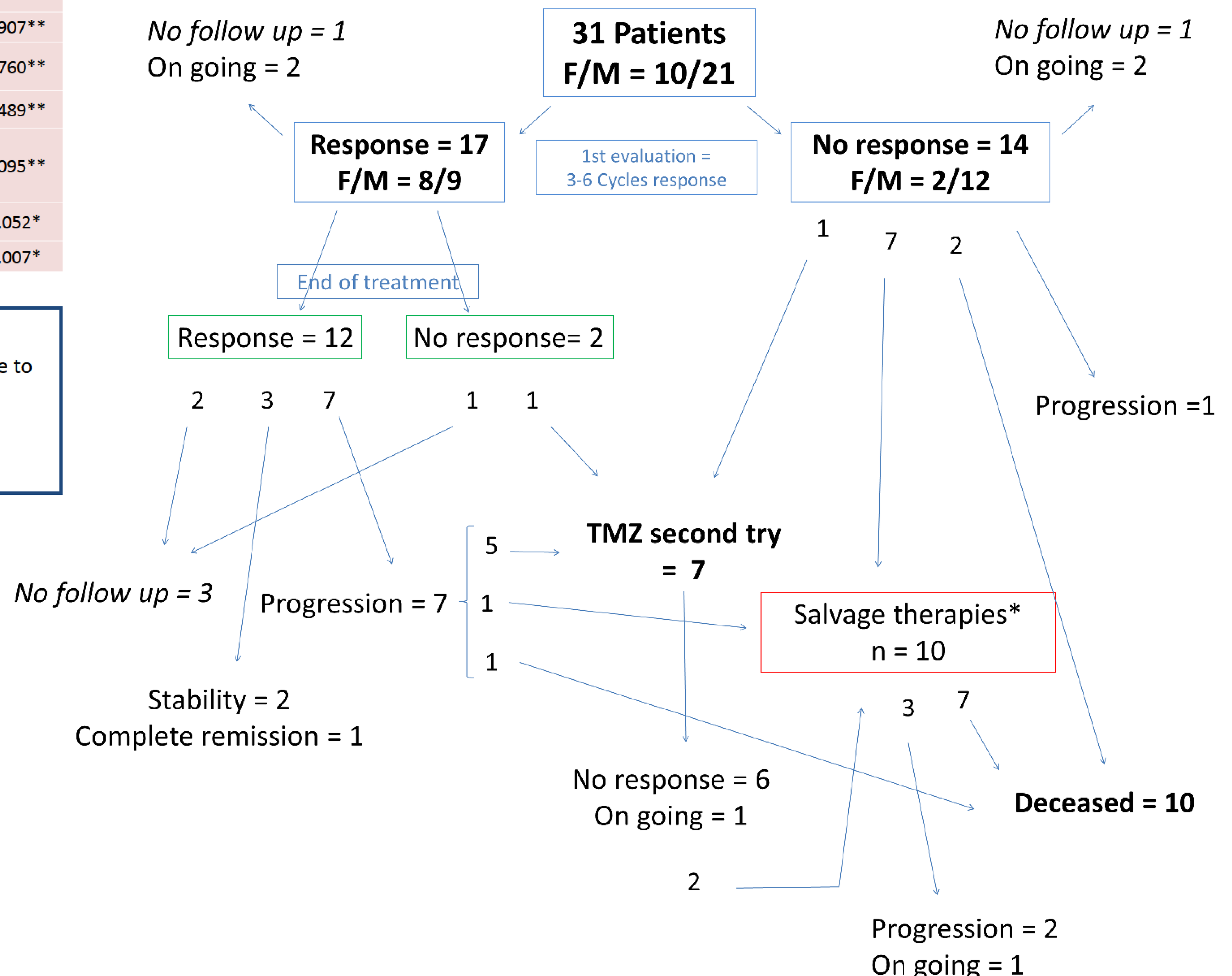
All second try of TMZ failed.

All salvage therapies* failed :

- Everolimus
- cisplatine/VP16, Carboplatine/VP16
- Folfox
- Xeloda
- CCNU
- Everolimus
- Lapatinib

Short term response	Long term response
3-6 cycles N = 31	End of treatment Median 7,5 cycles (5-24) N = 22
17/31 Hormonal n = 6 Tumoral = 6 Both = 5	**12/22** of whom 12 initial responders

Treatment flow-chart



**Conclusion : Initial pituitary tumors response to TMZ is frequent but long term control or remission are rare.
This survey underlined lack of homogeneous therapeutic protocol and the need for guideline.**

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