

Meningioma under progestin treatment : our experience

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Background

2007 : EPI-PHARE => increased risk of meningioma with

- Cyproterone acetate (Androcur[®])
- Nomegestrol acetate (Lutenyl[®], Nogest[®])
- Chlormadinone acetate (Lutéran[®], Helen[®])



Risk proportional to the cumulative dose (daily dosage + duration)

EMA (2020 and 2022) :

- Use of progestins at the minimally effective dose
- Mandatory discontinuation of progestins in case of meningioma

Our study

Inclusion criteria : female patients with meningioma seen in neurosurgery or gynecology-endocrinology at CHU Liège since January 2022

Prospective study

26 patients in prospective study

Constatations :

- Special characteristics of meningiomas
- Important cumulated doses of progestins
- Cases of stabilization or regression of the lesion after discontinuation of progestin treatment

Results

Median age : 48 (29-75) with 27% menopausal

88% undergoing hormonal therapy, 92% had progestins and 58% incriminated molecules

Preferred localization : **sphenoid (53,8%)** and frontal (30,7%) regions

Histologically : **meningothelial (78,5%)**, atypical (7,1%), both (7,1%), myxoid (7,1%)

WHO Grade : **grade I (85,7%)**, grade I and II (7,1%), II or III (7,1%)

Management : surgery +- radiotherapy (57,7%), radiotherapy only (3,8%), imaging follow-up only (38,5%)

Cumulative doses

N°	Type P	Molécule	Dose cumulée en g
1	Lutenyl	Acétate de nomegestrol	0,46
2	Androcur	Acétate de cyprotérone	18,77
3	Lutenyl	Acétate de nomegestrol	9,13
4	Lutenyl	Acétate de nomegestrol	9,13
5	Mercilon	Désogestrel	1,64
6	Lutenyl	Acétate de nomegestrol	7,3
7	/	/	/
8	Femoston low	Dydrogestérone	9,13
9	Utrogestan	Progestérone	365
10	Mirena	Lévonorgestrel	MIRENA
11	/	/	/
12	Lutenyl	Acétate de nomegestrol	5,48
13	Mirena	Lévonorgestrel	MIRENA
14	Noranelle	Lévonorgestrel	0,88
15	Lutenyl	Acétate de nomegestrol	34,22
16	Lutenyl	Acétate de nomegestrol	5,48
17	Mirena	Lévonorgestrel	MIRENA
18	Mirena	Lévonorgestrel	MIRENA
19	Helen	Acétate de chlormadinone	8,21
20	Lutenyl	Acétate de nomegestrol	22,8
21	Lutenyl	Acétate de nomegestrol	2,7
22	Lutenyl	Acétate de nomegestrol	54,8
23	Minulet + Lueva	Désogestrel + gestodène	0,57
24	COOP classique	Désogestrel	0,6
25	Utrogestan	Progestérone	10,1
26	Zoely	Acétate de nomegestrol	9,4

Cumulative dose of nomegestrol acetate	Incidence rate (in patient-years)	HRadj (95% CI) ^a	
Slightly exposed (≤0.15 g)	7.0/100,000	Ref.	
Exposed to > 0.15	19.3/100,000	4.5 [3.5-5.7]	
1.2 to 3.6 g	17.5/100,000	2.6 [1.8-3.8]	
3.6 to 6 g	27.6/100,000	4.2 [2.7-6.6]	
More than 6 g	91.5/100,000	12.0 [8.8-16.5]	

1,2 g = 18 months
5mg/d
14d/month

Cumulative dose of chlormadinone acetate	Incidence rate (in patient-years)	HRadj (95% CI) ^a	
Slightly exposed (≤0.36 g)	6.8/100,000	Ref.	
Exposed to > 0.36	18.5/100,000	4.4 [3.4-5.8]	
1.44 to 2.88 g	11.3/100,000	2.6 [1.4-4.7]	
2.88 to 5.76 g	12.4/100,000	2.5 [1.5-4.2]	
5.76 to 8.64 g	23.9/100,000	3.8 [2.3-6.2]	
More than 8.64 g	47.0/100,000	6.6 [4.8-9.2]	

1,44 g = 5 months
10mg/d
= 30 months
2mg/d
21j/month

Dose cumulée d'ACP	Taux d'incidence (en patient-années)	HR ^a _{ajusté} (IC à 95%) ^b	
Faiblement exposée (<3 g)	4,5/100 000	Réf.	
Exposée à ≥3 g	23,8/100 000	6,6 [4,0-11,1]	
12 à 36 g	26/100 000	6,4 [3,6-11,5]	
36 à 60 g	54,4/100 000	11,3 [5,8-22,2]	
Plus de 60 g	129,1/100 000	21,7 [10,8-43,5]	

12 g = 12 months
50mg/d
20d/month

ANSM 2020 : Restrictions d'utilisation de l'acétate de cyprotérone liées au risque de méningiome
EMA 2022 : Chlormadinone acetate and nomegestrol acetate: Measures to minimise the risk of meningioma

Conclusions

Risk-benefit balance of the treatment

If initiating treatment : use the **minimal effective dose** and **limit the duration** of use

Potential for **lesion regression or stabilization** after discontinuation of progestin
=> Avoiding surgical or radiotherapeutic interventions

Recently, medrogestone and medroxyprogesterone are incriminated too

Commission with AFMPS to report our cases

