Antitumour activity of MDV3100 in castration-resistant prostate cancer: a phase 1–2 study

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Objectifs

Principal

- Safety and tolerability profile of MDV3100
- To establish the maximum tolerated dose (MTD)

Secondaire

- Antitumour effects : PCWG2

Population

- Diagnosis of prostate cancer, histologically confirmed
- Progressive castration resistant disease :
  - castrate concentrations of testosterone (<1.7 nmol/L),
  - AND rising PSA
  - with or without detectable metastases.

Schéma d'escalade de dose 3+3

Phase I: 1er pt de la cohorte traité à J1, observé 6 jours puis prise en continue
Evaluation des toxicités à J28

	Total	No previous chemotherapy	Previous chemotherapy
30 mg per day	3	3	0
60 mg per day	27	15	12
150 mg per day	28	15	13
240 mg per day	29	17	12
360 mg per day	28	15	13
480 mg per day	22	0	22
600 mg per day	3	0	3
Total	140	65	75

Data are number of patients enrolled.

Phase II: Du fait de la réponse biologique des 6ers pts:
extension de toutes les cohortes de 60 à 360 mg de 24 patients suplémentaires

Suivi des toxicités

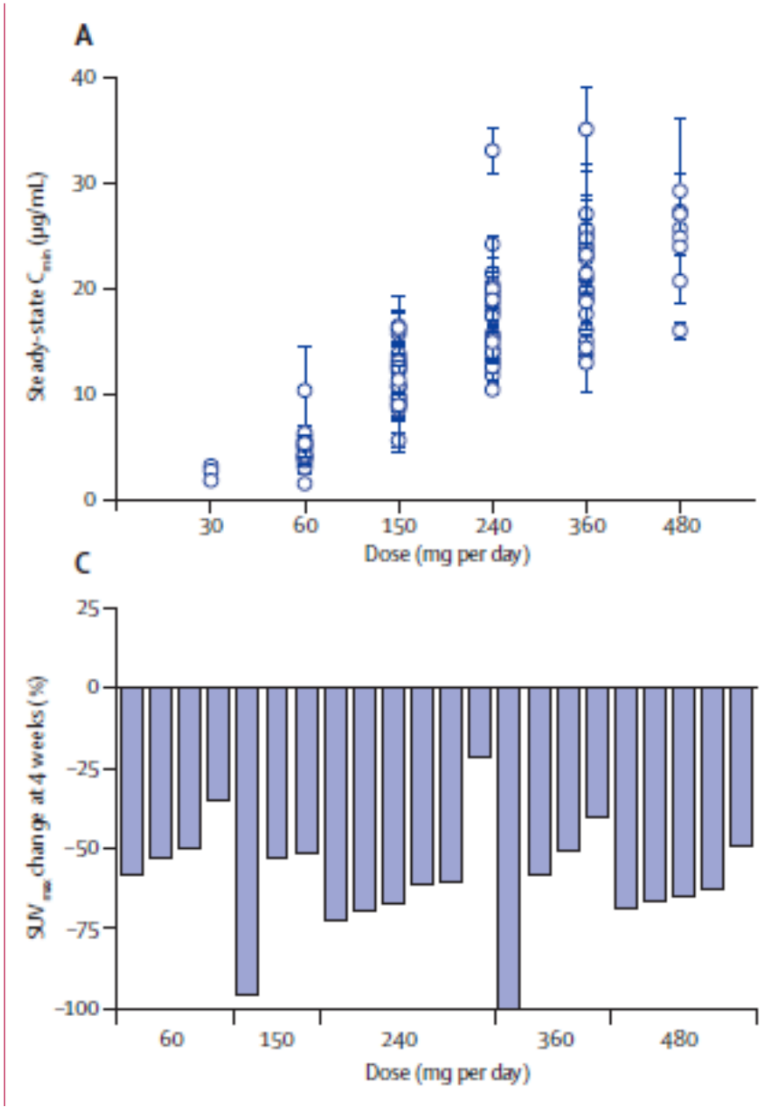
Critères NCI CTCAE VERSION 3.0

	30 mg per day (n=3)	60 mg per day (n=27)	150 mg per day (n=28)	240 mg per day (n=29)	360 mg per day (n=28)	480 mg per day (n=22)	600 mg per day (n=3)	Total (n=140)
Grade 3–4 adverse events occurring in more than two patients								
Fatigue	0	0	0	5 (17%)	6 (21%)	5 (23%)	0	16 (11%)
Anaemia	0	2 (7%)	1 (4%)	0	1 (4%)	0	0	4 (3%)
Arthralgia	0	2 (7%)	0	0	0	1 (5%)	0	3 (2%)
Asthenia	0	0	0	0	2 (7%)	1 (5%)	0	3 (2%)
Seizure	0	0	0	0	1 (4%)	1 (5%)	1 (33%)	3 (2%)
Adverse events leading to discontinuation of treatment								
Seizure	0	0	0	0	1 (4%)	1 (5%)	1 (33%)	3 (2%)
Rash	0	0	0	0	0	1 (5%)	1 (33%)	2 (1%)
Nausea/vomiting	0	0	0	0	0	1 (5%)	0	1 (1%)
Fatigue	0	0	0	1 (3%)	0	0	0	1 (1%)
Myocardial infarction	0	0	0	0	1 (4%)	0	0	1 (1%)

Data are number (%) of patients.

Table 5: Grade 3–4 adverse events and patients who discontinued treatment because of an adverse event, by dose

Pharmacokinetics and pharmacodynamics of MDV3100



- MTD:
  - 240 mg
- Dose recommandée pour la suite des études:
  - 160 mg basée sur la relation toxicité/efficacité des différentes études