Projet d'érudition

Un court cycle d'insulinothérapie intensive comme traitement initial du diabète de type 2 pour induire une rémission glycémique prolongée

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Diabète de type 2

- Le diabète de type 2 en médecine familiale
- Déclin progressif de la fonction cellules β du pancréas (glucotoxicité, lipotoxicité)
- Approche actuelle de traitement

Question PICO

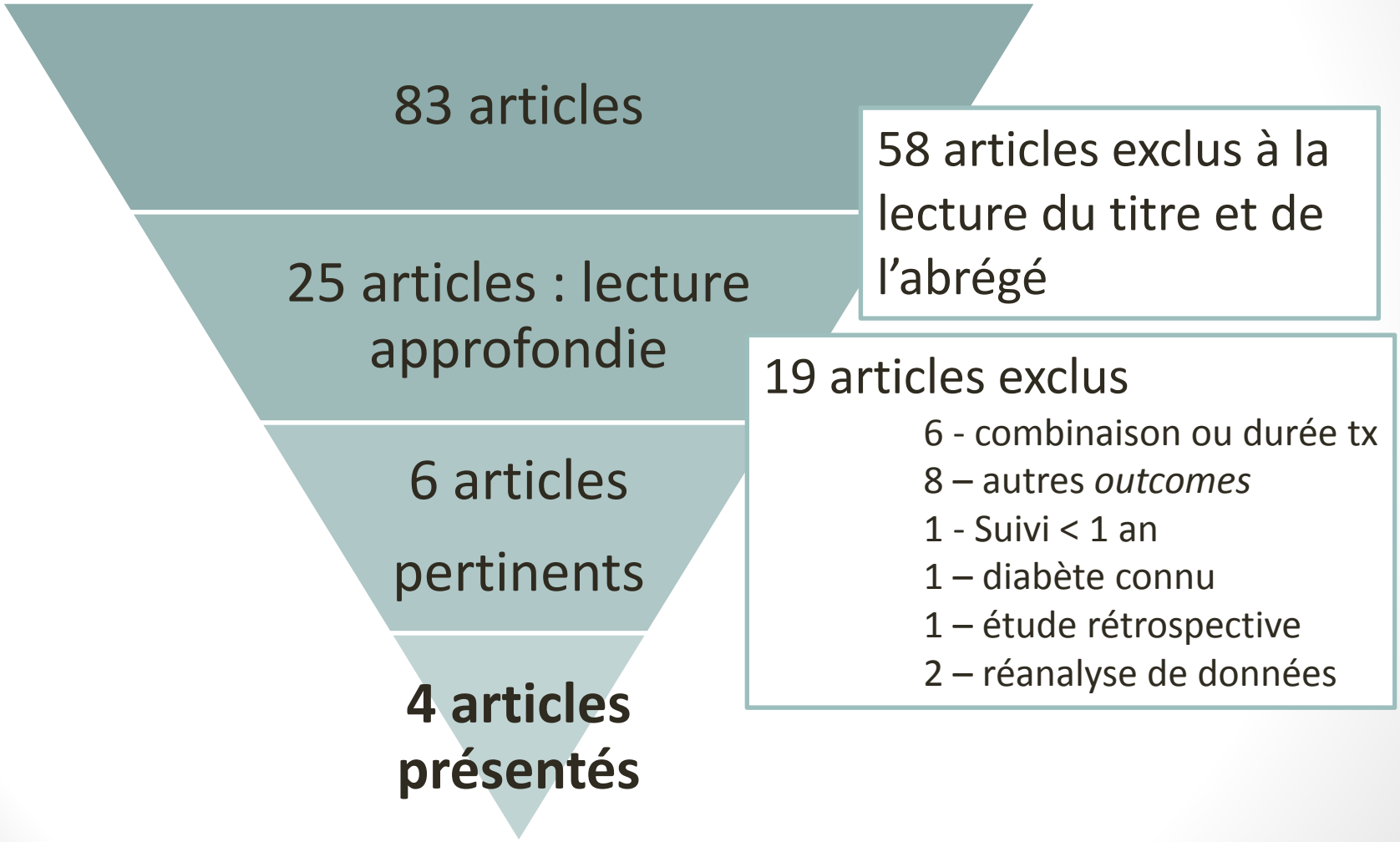
Peut-on établir un **contrôle glycémique à long terme** sans médication (rémission) chez des patients adultes avec un **diabète de type 2 nouvellement diagnostiqué** à l'aide d'une **insulinothérapie intensive de courte durée** ?

Recherche

- Recherche dans Pubmed/MEDLINE avec les termes:
  - “newly diagnosed type 2 diabetes intensive insulin”

- Critères d’inclusion
- Critères d’exclusion

Recherche


83 articles
25 articles : lecture approfondie
6 articles pertinents
4 articles présentés
58 articles exclus à la lecture du titre et de l'abrégé
19 articles exclus
6 - combinaison ou durée tx
8 – autres *outcomes*
1 - Suivi < 1 an
1 – diabète connu
1 – étude rétrospective
2 – réanalyse de données

Article 1

Ilkova H, Glaser B, Tunckale A, Bagriacik N, Cerasi E.

Induction of long-term glycemic control in newly diagnosed type 2 diabetic patients by transient intensive insulin treatment.

1997

American Diabetes Association. Diabetes Care

Article 1 – Résultats

Évolution des 13 patients

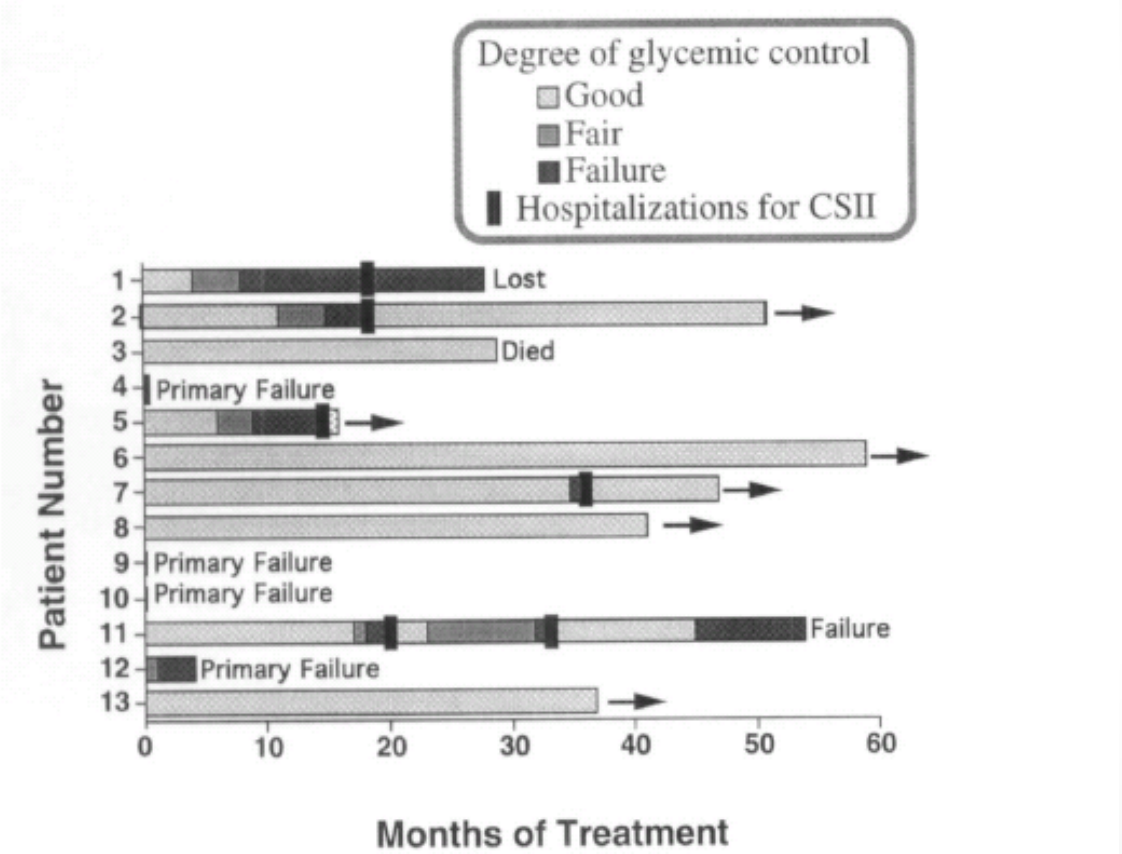
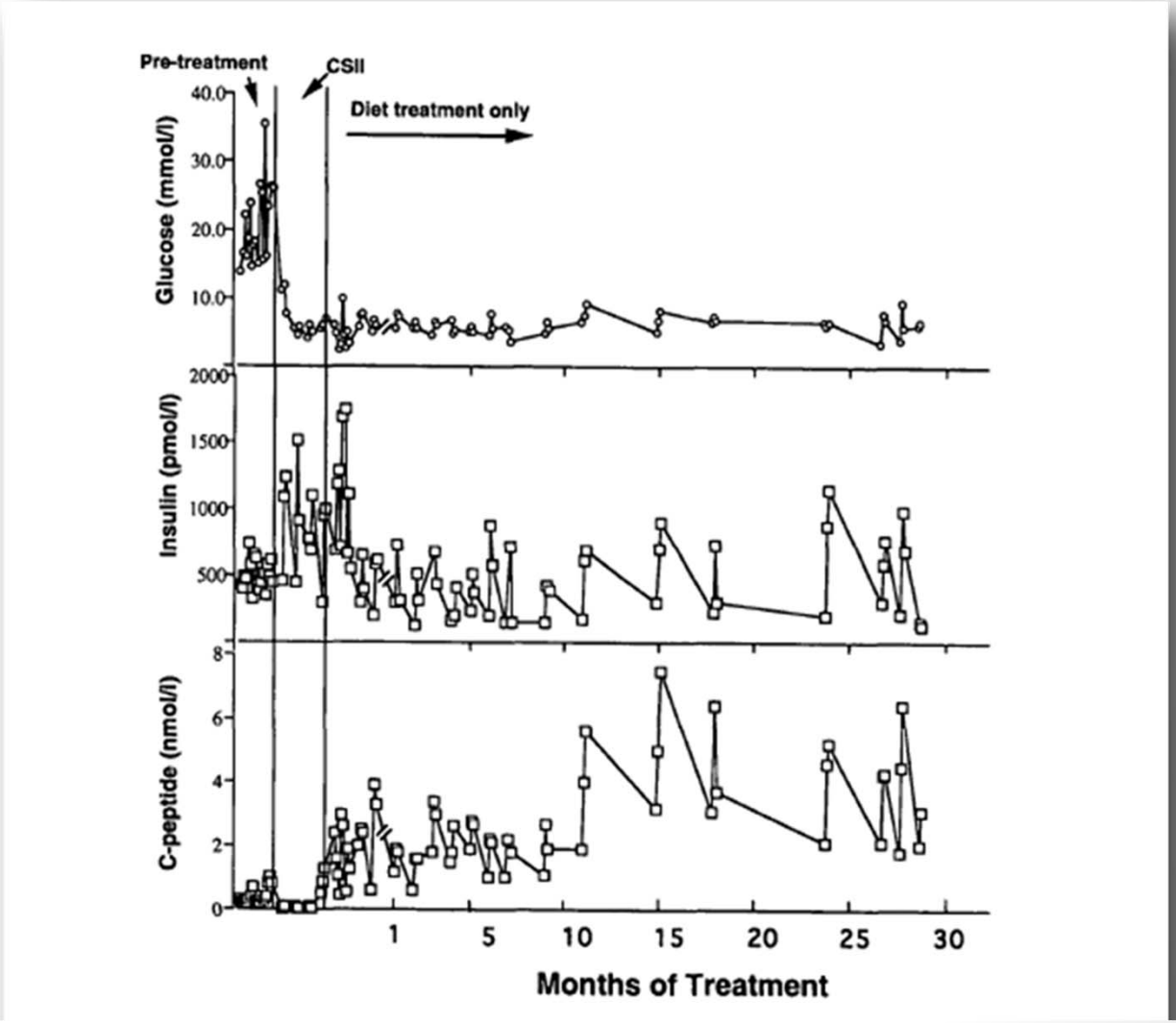


Figure 1—*Long-term follow-up of 13 patients. See results for a description of individual patients and Table 1 for a summary.*

Article 1 – Résultats

Patient 8
(figure 2)



Article 2

Ryan EA, Imes S, Wallace C.

Short-term intensive insulin therapy in newly diagnosed type 2 diabetes

2004

American Diabetes Association. Diabetes Care

Article 2 – Résultats

- 44% de rémission à 1 an (7/16)
- ↓ Glycémie à jeun
- ↑ Sécrétion d'insuline (HGOP)

Table 1—*Measures of glycemia and insulin secretion, lipids, and body weight before insulin therapy, directly after insulin therapy, and at 1-year follow-up*

	Before insulin treatment	After insulin treatment	1 Year
Fasting serum glucose (mmol/l)	13.3 ± 0.7	7.0 ± 0.4*	6.7 ± 0.3†
HbA_{1c} (%)	11.8 ± 0.3	—	6.6 ± 0.3†
Fructosamine (μmol/l)	428 ± 38	286 ± 15*	288 ± 11†
AUC_g (mmol · min)	1,176 ± 66	1,184 ± 65	916 ± 53†¶
Fasting serum insulin (pmol/l)	84.7 ± 10.8	97.6 ± 12.2	108.3 ± 15.1
Fasting C-peptide (μg/l)	1.04 ± 0.36	1.27 ± 0.29	—
AUC_i (pmol · min)	8,251 ± 1,880	18,404 ± 4,040	42,368 ± 8,517†¶
Total cholesterol (mmol/l)	6.16 ± 0.42	—	4.72 ± 0.28†
Triglycerides (mmol/l)	3.90 ± 0.72	—	2.08 ± 0.39†
Free fatty acids (mmol/l)	1.1 ± 0.10	0.76 ± 0.10	0.64 ± 0.08§
BMI (kg/m²)	30.8 ± 1.9	30.9 ± 1.9	30.3 ± 1.8§

Data are means ± SE. *$P < 0.01$ significant difference of before versus after insulin treatment; †$P < 0.01$ significant difference of before versus after 1 year; ¶$P < 0.01$ significant difference of after insulin treatment versus 1 year; and §$P < 0.05$ significant difference after insulin treatment versus 1 year.

Article 2 – Résultats

AUC_i = aire sous la courbe = sécrétion insuline

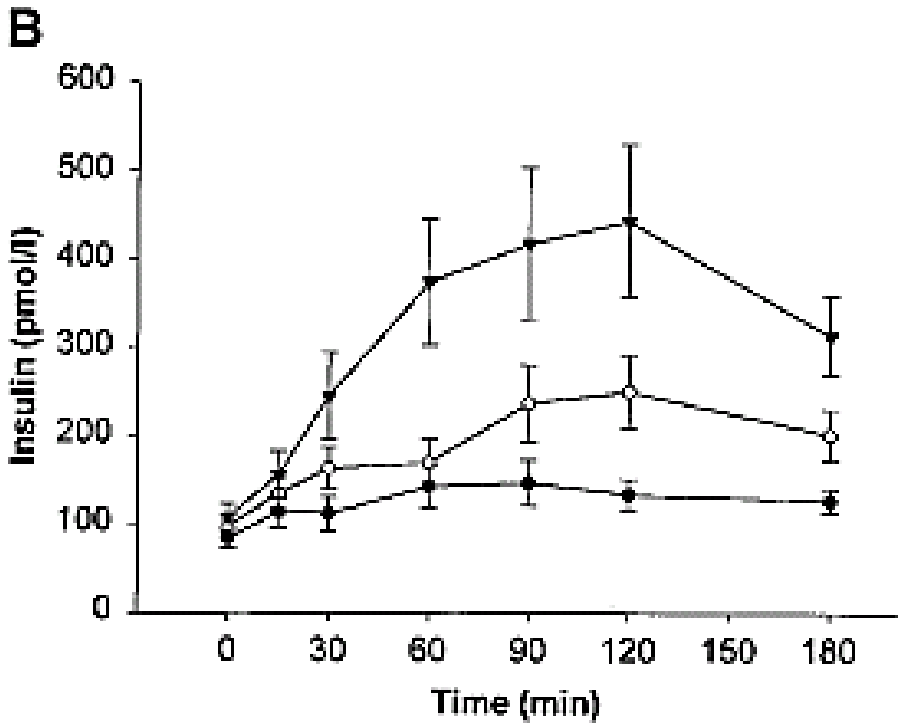


Figure 1—*Means ± SE for serum glucose (A) and insulin (B) concentrations during OGTT before insulin therapy (●, n = 16) immediately after insulin therapy (○, n = 16) and at 1-year follow-up (▼, n = 14). Both the AUC_g (mmol · min) and the AUC_i (pmol · min) at 1 year were significantly different from the values before and directly after insulin therapy ($P < 0.01$).*

Article 2 – Résultats

- Paramètres différents entre les groupes ?
  - Glycémie AC avant/après
  - Dose insuline nécessaire

Table 2—*Clinical and biochemical characteristics at baseline or at the end of the initial insulin therapy of the group maintained on diet alone versus those requiring OHA or insulin on long-term follow-up*

	Diet only	OHA/insulin
n	7	9
BMI (kg/m^2) before insulin therapy	29.0 ± 2.1	32.2 ± 2.9
Waist-to-hip ratio before insulin therapy	0.98 ± 0.02	1.01 ± 0.02
Fasting serum glucose before insulin therapy (mmol/l)	13.2 ± 0.8	13.3 ± 1.1
Fasting serum glucose after insulin therapy (mmol/l)	5.9 ± 0.3	7.7 ± 0.4*
HbA_{1c} before insulin (%)	12.3 ± 0.5	11.5 ± 0.5
Fasting insulin before insulin therapy (pmol/l)	82.4 ± 16.5	86.7 ± 14.9
Fasting C-peptide before insulin therapy (μg/l)	0.96 ± 0.31	1.10 ± 0.62
Free fatty acids before insulin therapy (mmol/l)	0.94 ± 0.18	1.18 ± 0.11
AUC_i before insulin therapy (pmol · min)	7,937 ± 3,983	8,498 ± 1,576
AUC_i after insulin therapy (pmol · min)	17,870 ± 6,175	18,821 ± 5,661
Insulin dose required during intensive therapy (unit · kg^{-1} · day^{-1})	0.37 ± 0.05	0.73 ± 0.07*

Data are means ± SE. *Significant difference of group maintained on diet only versus those requiring OHA or insulin ($P < 0.01$).

Article 3

Li Y, Xu W, Liao Z, et al.

Induction of long-term glycemic control in newly diagnosed type 2 diabetic patients is associated with improvement of β-cell function.

2004

American Diabetes Association. Diabetes Care

Article 3 – Résultats

- 113 patients suivis
  - 47.1% de rémission à 1 an (et 42.3 % à 2 ans)
  - Amélioration du HOMA-B et HOMA-IR

N=126	Avant insuline	Après insuline
HOMA-B	36.1 ± 25.1	121.3 ± 96.3
HOMA-IR	8.3 ± 4.1	4.3 ± 3.4

Article 4

Weng J, Li Y, Xu W, et al.

Effect of intensive insulin therapy on β-cell function and glycaemic control in patients with newly diagnosed type 2 diabetes: a multicentre randomised parallel-group trial.

2008

THE LANCET

Article 4 – Résultats

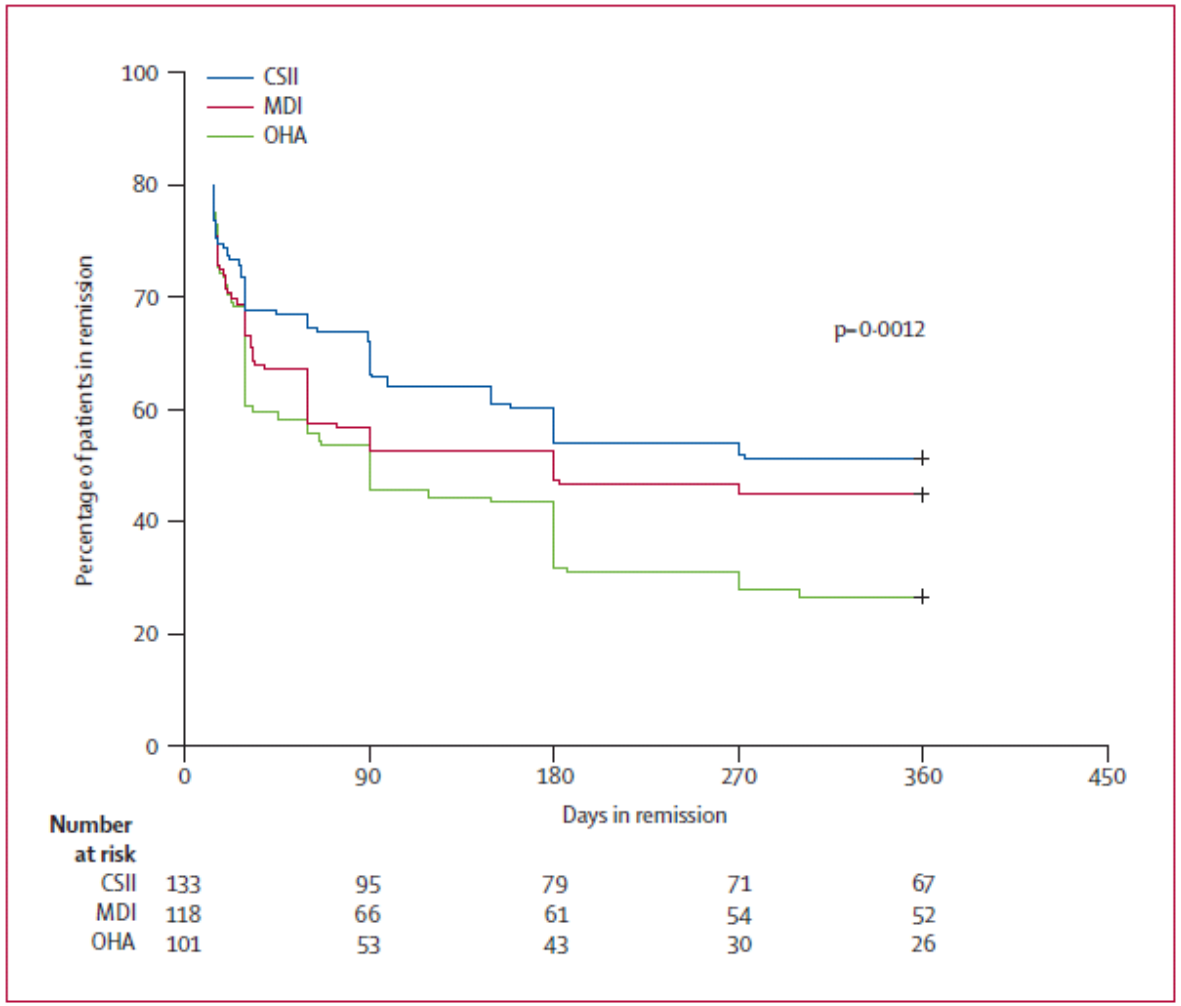


Figure 2: **Kaplan-Meier estimates of time to primary endpoint**

Rémission à 1 an

- Pompe 51.1%
- Injections 44.9%
- HGO 26.7%

Discussion

- 41 à 51% de rémission à 1 an
- Forces et limites des études
- Interprétation personnelle

Conclusion

Références

1. Ilkova H, Glaser B, Tunckale A, Bagriacik N, Cerasi E. Induction of long-term glycemic control in newly diagnosed type 2 diabetic patients by transient intensive insulin treatment. Diabetes Care 1997; 20: 1353–56.
2. Ryan EA, Imes S, Wallace C. Short-term intensive insulin therapy in newly diagnosed type 2 diabetes. Diabetes Care 2004; 27: 1028–32.
3. Li Y, Xu W, Liao Z, et al. Induction of long-term glycemic control in newly diagnosed type 2 diabetic patients is associated with improvement of β-cell function. Diabetes Care 2004; 27: 2597–602.
4. Weng J, Li Y, Xu W, et al. Effect of intensive insulin therapy on β-cell function and glycaemic control in patients with newly diagnosed type 2 diabetes: a multicentre randomised parallel-group trial. Lancet 2008; 371: 1753–60.

- Matthews et al. "Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man.".1985 *Diabetologia* **28** (7): 412–9.

Aux superviseurs, collègues et amis

Merci!