DIABETIC PERIPHERAL NEUROPATHIC PAIN

Optimizing DPNP management:

Actionable insights from the OPTION-DM trial

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Disclosure statement

This slide deck is a professional portfolio sample developed to demonstrate medical writing expertise. No industry funding or support was received for the creation of this material.

All data is derived from the peer-reviewed OPTION-DM trial published in *The Lancet*.

The challenge of DPNP: when monotherapy reaches a ceiling

Prevalence

Diabetic peripheral neuropathy affects about 50% of people with diabetes, and approximately half of these present with **neuropathic pain.**

Treatment limitations

Current guidelines recommend **Amitriptyline**, **Duloxetine**, or **Pregabalin** as first-line agents.

However, the best outcome for any first-line agent is just **50% pain relief** in fewer than **half of patients.**

The gap

Despite clinicians' widespread use of combination therapy, there was **no robust clinical evidence** to inform guidelines.

This is why the Optimal Pathway for TreatIng neurOpathic paiN in Diabetes Mellitus **(OPTION-DM)** trial was funded in 2015.

CHALLENGE

To optimize treatment outcomes, clinicians needed answers to **two fundamental questions:**

1. Which first-line drug should be **prescribed first**?

2. What should be added when **monotherapy falls** short?

OPTION-DM: the 3 x 3 crossover design

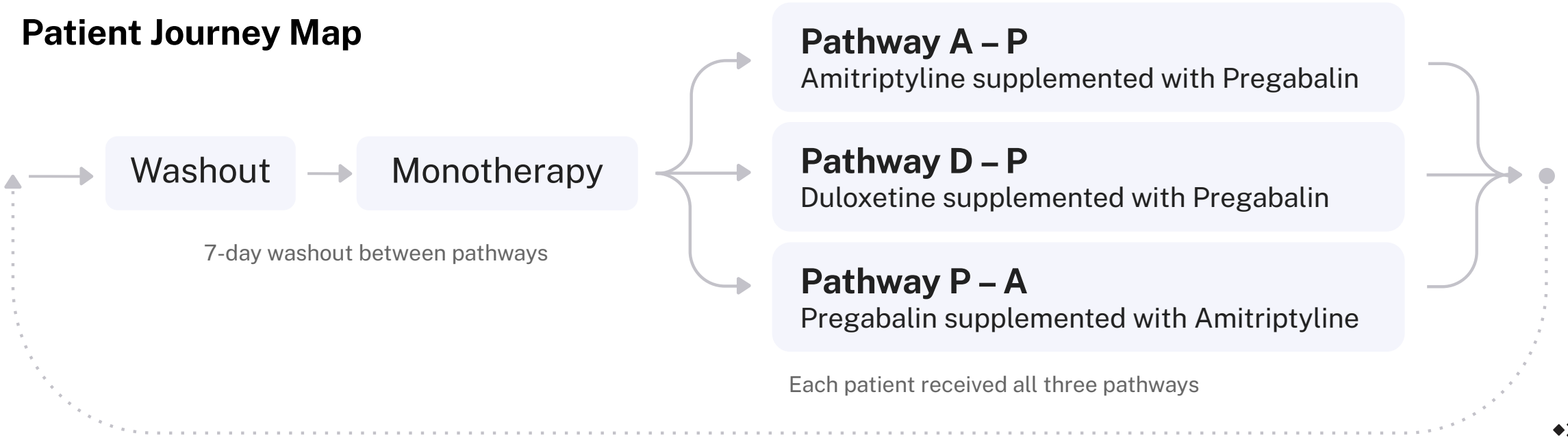
130
Patients

Multicentre
Double-blind

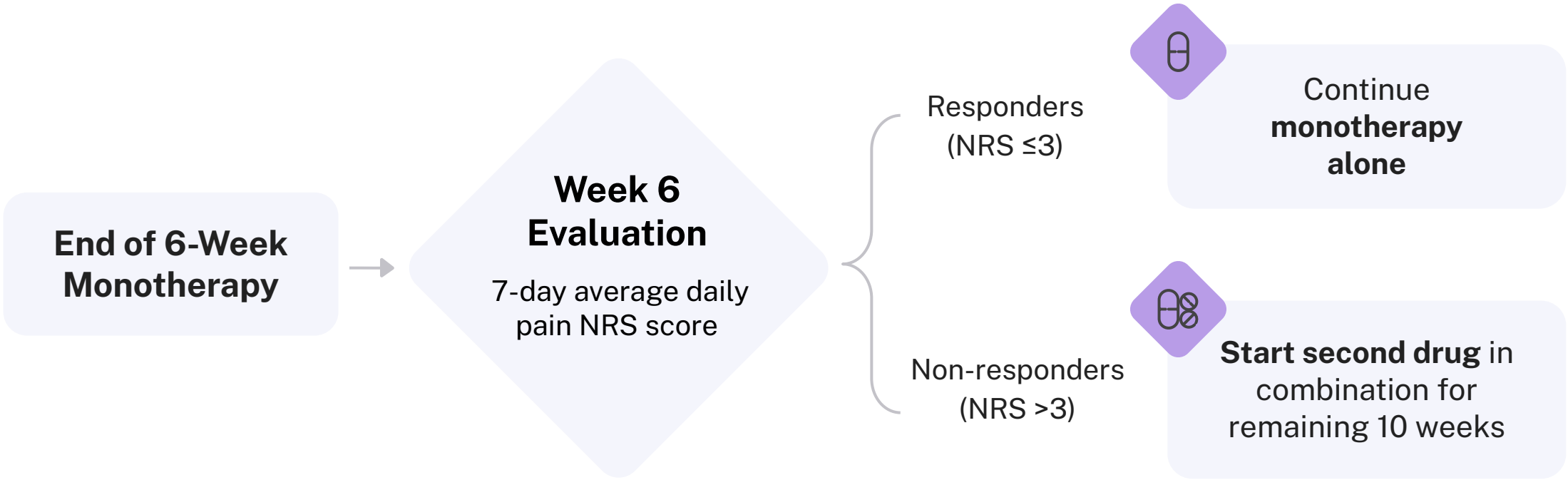
50 weeks
Total Duration

Active
Washouts

Patient Journey Map

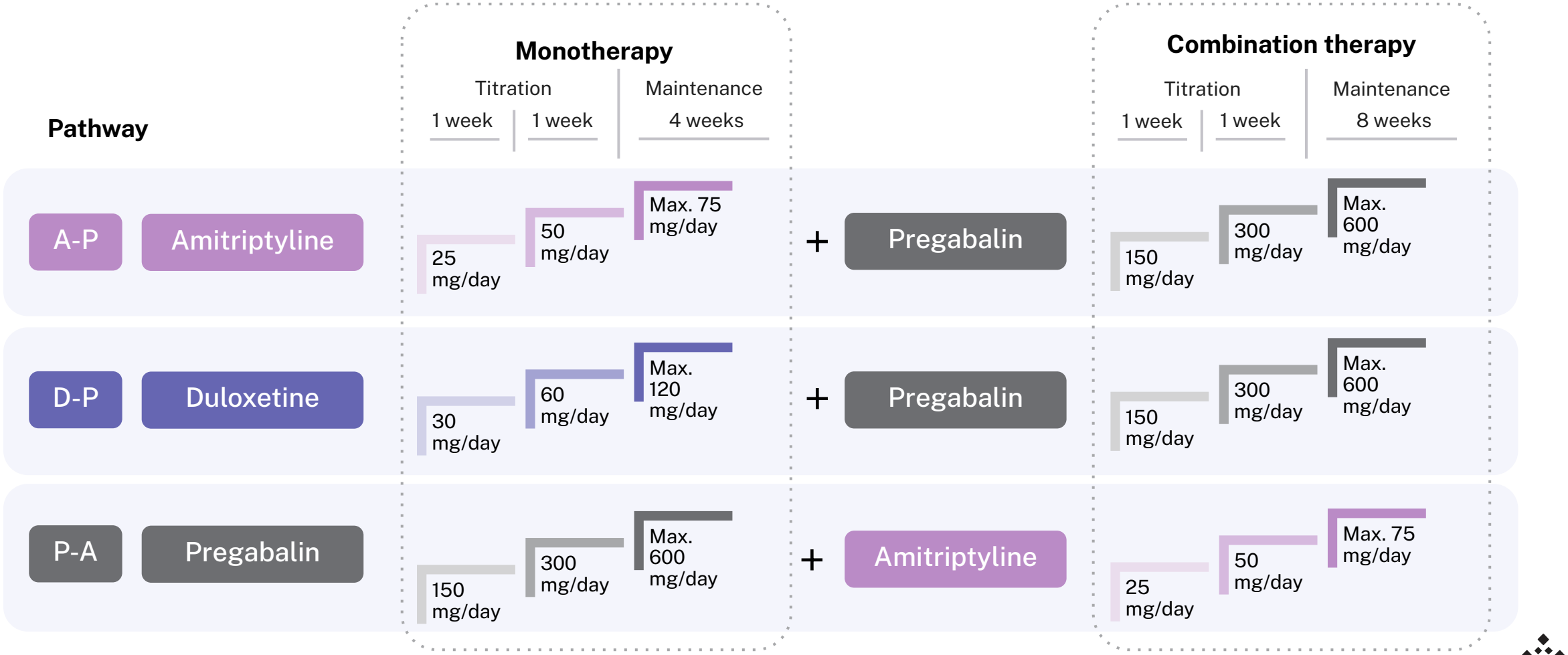


A practical approach to DPNP management



The OPTION-DM trial design explicitly mimics real-world practice, testing not only a drug but a complete treatment pathway.

The escalation protocol: from monotherapy to targeted combination



For patients with impaired renal function (eGFR 30–59 ml/min/1.73m^2), the **maximum dose of pregabalin** was 300 mg/day.

BASELINE

A representative DPNP population

Demographics

- Age: 61 (55 – 70) years
- Males: 96 (74%)
- BMI: 32 (6.6) kg/m^2

Previous medication

- Amitriptyline: 49 (38%)
- Duloxetine: 47 (36%)
- Pregabalin: 45 (35%)
- Gabapentin: 44 (34%)
- Any opioids: 47 (36%)

Diabetes characteristics

- Type 1: 22 (17%)
- Duration of diabetes: 15.1 (9.3) years
- Duration of neuropathic pain: 4.9 (4.1) years

Pain intensity

- NRS pain*: **6.6** (1.5)

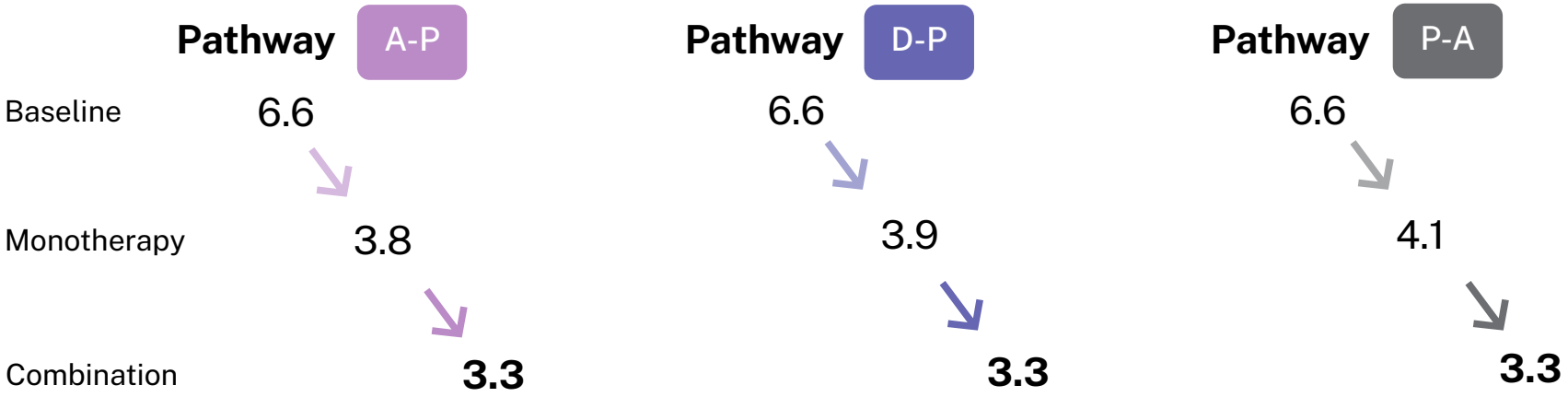
*Scale of 0–10; higher scores indicate greater pain.

PRIMARY OUTCOME

No statistically or clinically significant difference between pathways, whether as monotherapy or in combination

Equivalence in efficacy allows for treatment **individualization** based on patient profiles

NRS* at the end of monotherapy (week 6) and combination treatment (week 16)



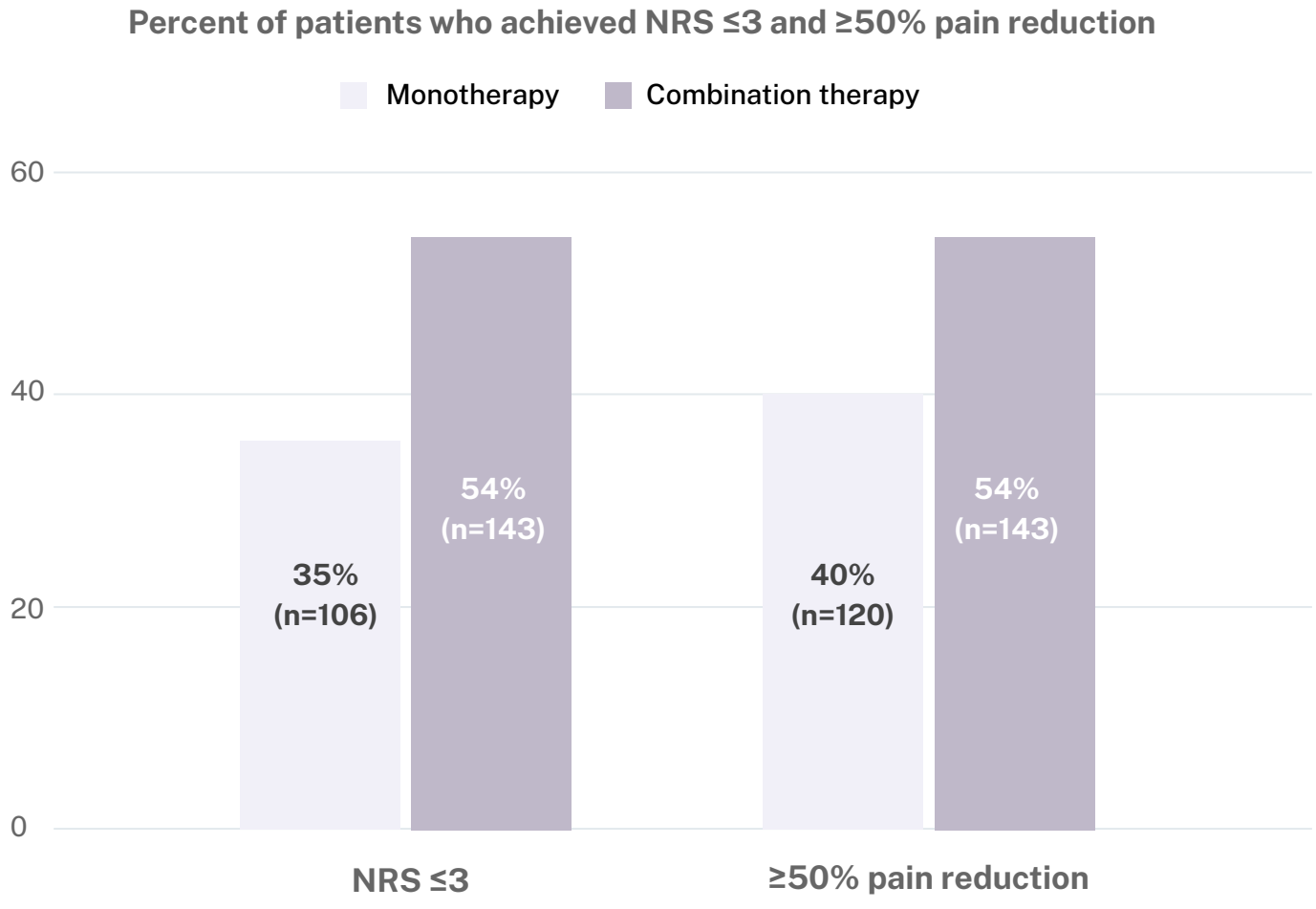
*NRS: numerical rating scale; NRS pain is rated on a scale of 0–10, with increasing numbers indicating increasing pain.

THE POWER OF COMBINATION

Improved pain reduction when monotherapy is insufficient

14% more patients achieved >50% pain relief with combination therapy *vs.* monotherapy.

Combination provided an additional **1.0-point drop** in pain (p<0.001).



Percentages at 6 weeks of monotherapy and after combination therapy at 16 weeks

Adverse events differentiate pathways

P-A has the lowest **discontinuation rate** (5%; p=0.031), compared to A-P (11%) and D-P (17%).

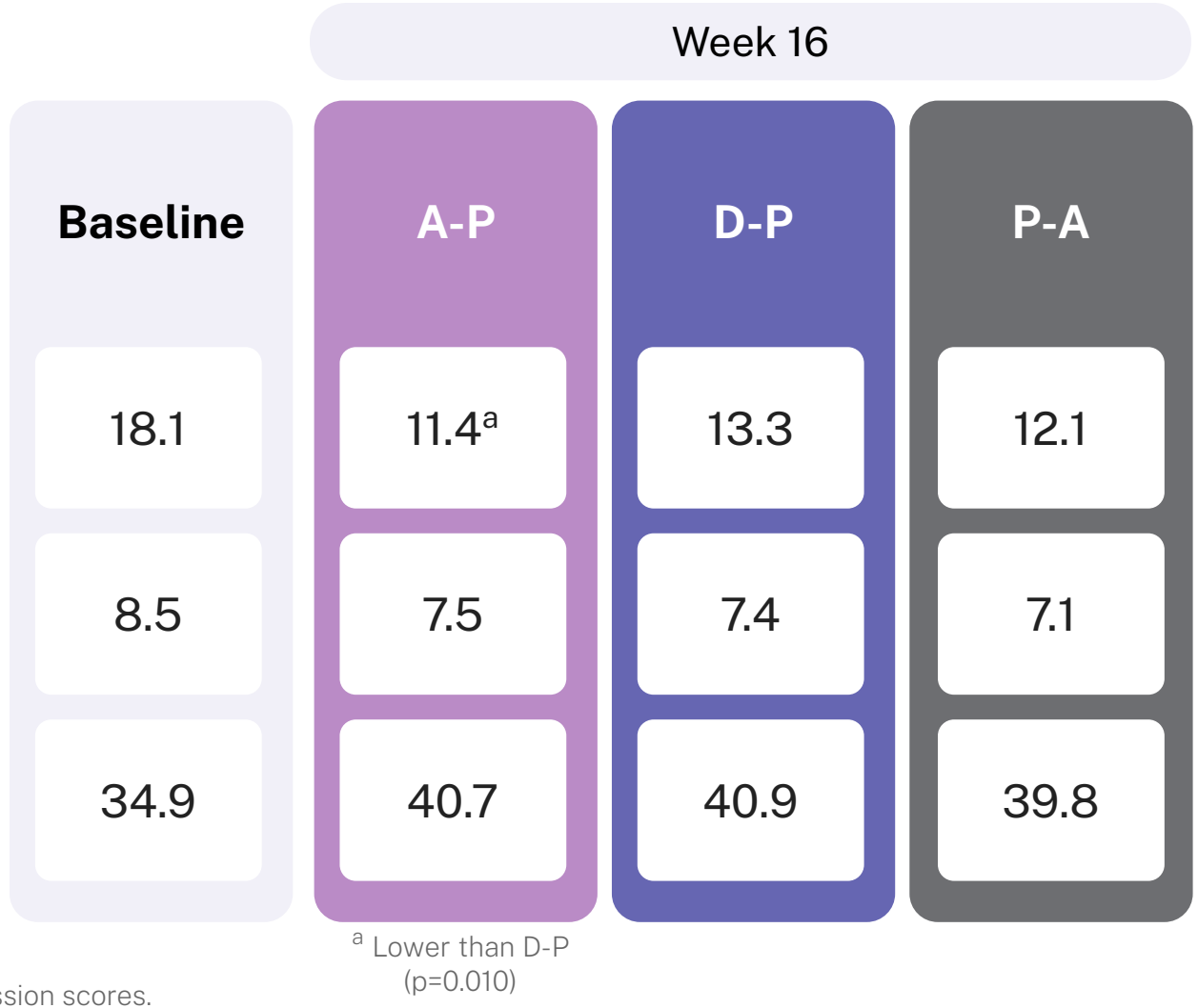
TEAE	Pathway A-P	Pathway D-P	Pathway P-A
 Dry mouth	**32%**	8%	17%
 Nausea	5%	**23%**	7%
 Dizziness	12%	15%	**24%**

Statistically significant treatment-emergent adverse events (TEAE) during the trial (week 0-16).

BEYOND PAIN SCORES

Impact on patient quality of life (QoL)

All pathways showed **similar improvements from baseline** in sleep quality, anxiety, depression, and overall physical functioning.



[a] Lower than D-P (p=0.010)

* Calculated mean of the combined HADS anxiety and depression scores.

Equal pain relief allows treatment individualization from day one

Select the initial agent to leverage benign side-effect and tolerability profiles:

Patient characteristic	Prioritize	Rationale from OPTION-DM findings
Insomnia	Amitriptyline	Amitriptyline was significantly better at improving sleep quality
Nausea	Amitriptyline or Pregabalin	Nausea was associated with Duloxetine
Dry Mouth	Duloxetine or Pregabalin	Dry mouth was associated with Amitriptyline
Balance / Fall Risk / Elderly	Amitriptyline or Duloxetine	Dizziness was frequent with Pregabalin
Anxiety / Depression	Pregabalin or Duloxetine	Patients with higher baseline HADS had a greater reduction in pain scores when starting on P-A or D-P compared to A-P
High Attrition / Medication Discontinuation Risk	Pregabalin	Significantly fewer treatment discontinuations caused by TEAEs

The OPTION-DM pathway: a standardized clinical algorithm

1. Start

- **Choose** the first drug according to the patient's profile

2. Escalate

- **Escalate** to the maximum tolerated dose to establish true monotherapy efficacy
- **Assess pain** at week 6

3. Combine

- **If NRS remains >3**:
- In patients who started with pregabalin: add **amitriptyline**
- In patients who started with amitriptyline or duloxetine: add **pregabalin**

Transformative takeaways for DPNP

1. 

All three first-line mono-therapies (Amitriptyline, Duloxetine, and Pregabalin) demonstrate **similar efficacy** in pain relief in patients with DPNP.

2. 

When monotherapy falls short, **combinations** of these first-line drugs **are safe**, well-tolerated, and effective.

3. 

Selecting an initial treatment option can be tailored based on the **patient's specific comorbidities,** emotional profile, tolerability risks, and affordability.

Reference

THE LANCET

Tesfaye S, Sloan G, Petrie J et al.
Comparison of amitriptyline supplemented with pregabalin, pregabalin supplemented with amitriptyline, and duloxetine supplemented with pregabalin for the treatment of diabetic peripheral neuropathic pain (OPTION-DM): a multicentre, double-blind, randomised crossover trial.

The Lancet, 2022; 400, 680-690.

Access the full analyses in *The Lancet* here.

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