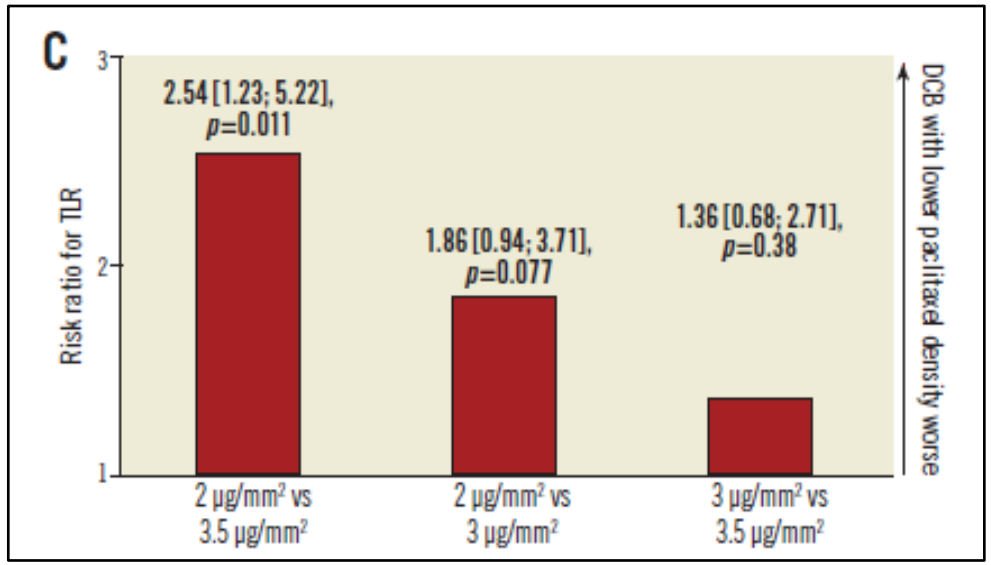
Novel double-dose DCB (6 µg/mm²)

- DCBs play an important role in the treatment of PAD by reducing restenosis
- The risk of restenosis in '**difficult-to-treat' lesions** is increased despite DCB use
- It is **unlikely that only one dose for all patients fits all clinical needs**
  → Higher drug dose might be necessary for patients with e.g.,
    - Severely calcified vessels
    - Diabetes mellitus
    - In-stent restenosis, restenosis after DCB/POBA
    - Occluded vessels
- So far, there is no dose-finding clinical trial for DCB treatment

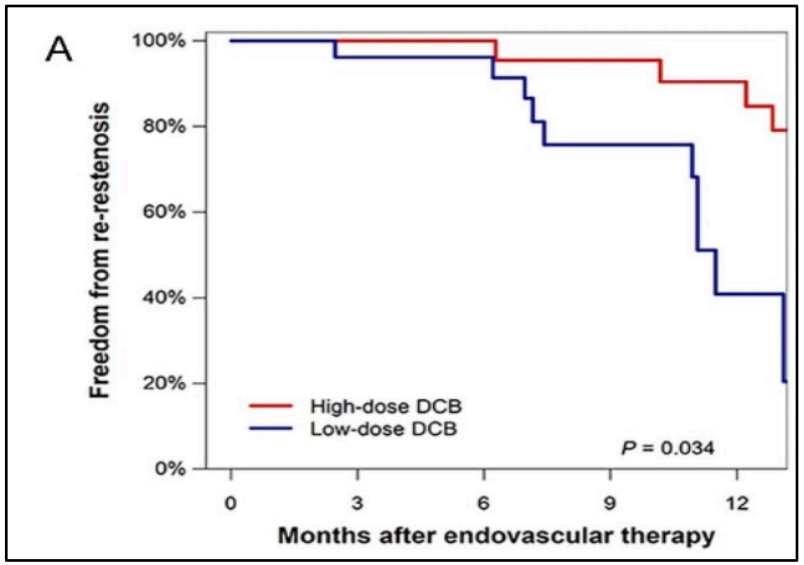
Rationale

Dose effect of DCB therapy



Result of meta-analysis of 20 randomized clinical trials including 5 trials (3 products) on 2 µg/mm², 9 trials (6 products) on 3 µg/mm², 7 trials (1 product) on 3.5 µg/mm²; de novo or restenotic FemPop.

Cassese et al.,
Euro Intervention 2019;15:e560-e562



High-dose DCB repetition vs. low-dose DCB repetition in FemPop restenosis; single-center, observational, 89 cases → freedom from re-restenosis: 90.4% vs. 40.9%.

Tomoi et al., Journal of Endovascular Therapy 2025, Vol. 32(4). 1102-1108

Rationale

COPA CABANA TRIAL

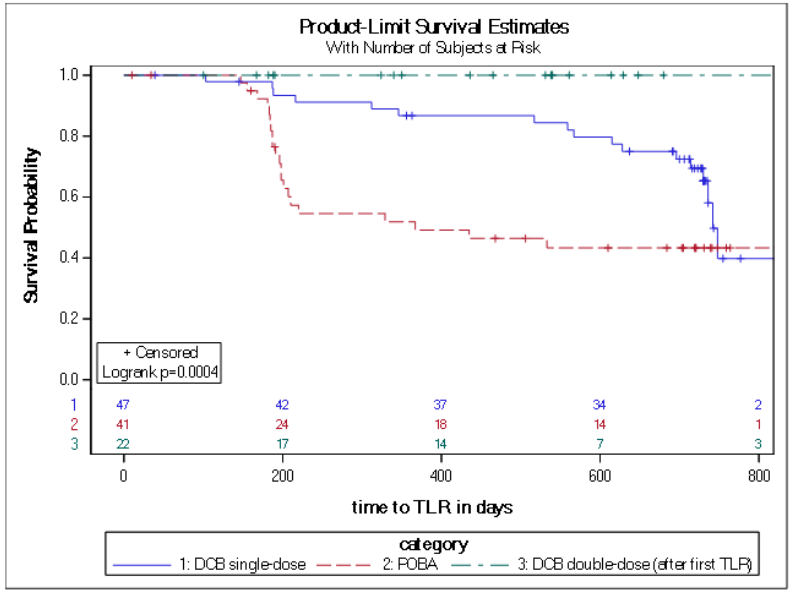
First study which suggested a **dose effect** of DCB therapy

88 patients with Fem-Pop binary in-stent restenosis (DCB vs. POBA)

- 22 patients with second in-stent restenosis (either after DCB or POBA)

→ Treatment with **2 fully overlapping DCB**s with 3 µg paclitaxel (Ptx)/mm²

- 6 months: **smaller late lumen loss (LLL) vs. single-dose and POBA**
  (0.11 ± 0.78 mm / 0.34 ± 1.12 mm / 1.58 ± 1.00 mm)
- 2 years: **no target lesion reinterventions vs. 52 % in single-dose group**
- **No adverse events** after double-dose treatment up to 20.6 ± 9.4 months



Tepe et al. J Endovasc Ther. 2020;27(2):276-86.

Aim: one DCB with a double dose paclitaxel (6 µg/mm²)

First double-dose DCB with 6 µg Ptx/mm²

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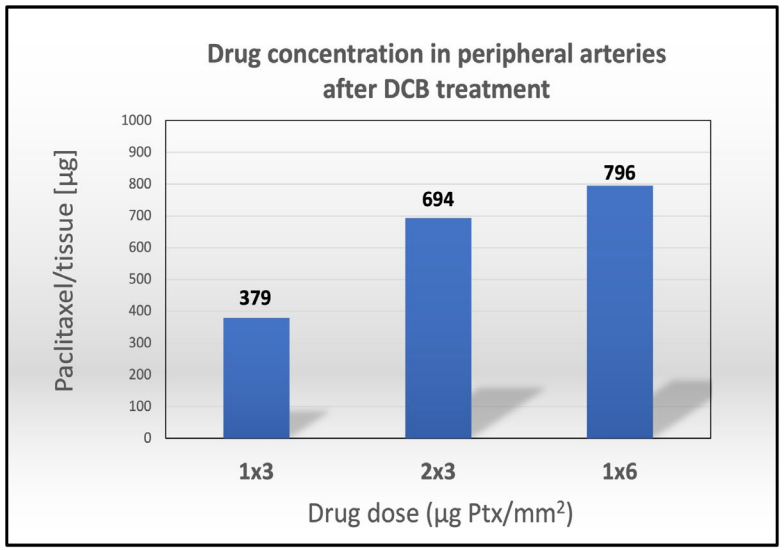
Preclinical studies (swine, peripheral arteries)

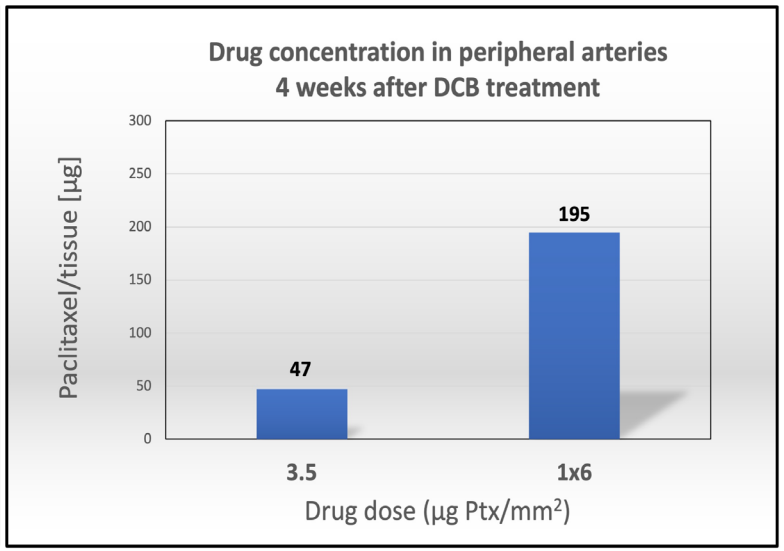
Drug uptake - acute



Double-dose DCB enabled to **double the drug uptake** to the vessel wall compared to a single dose (same coating formulation).

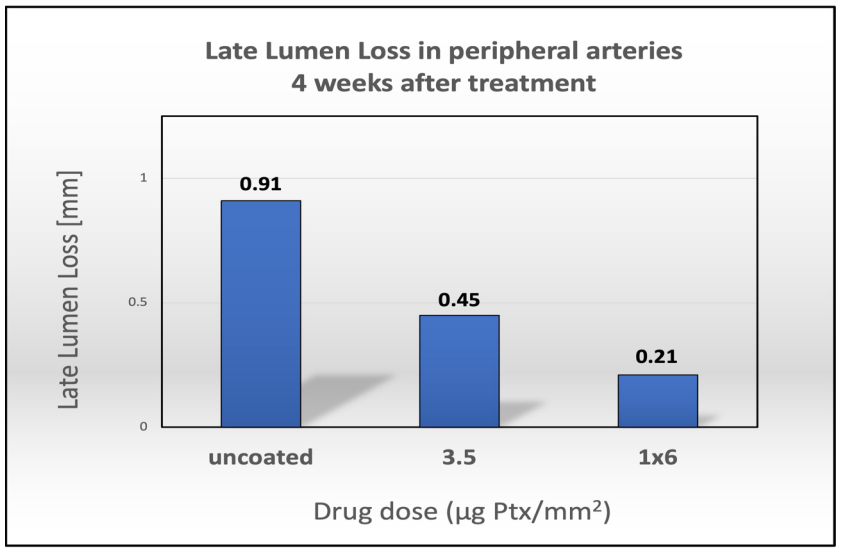
Gemeinhardt et al.. PLoS One. 2021;16(10):e0259106.

Drug uptake - 4 weeks



Double-dose DCB enabled a **four times higher drug amount** in the vessel wall 4 weeks after treatment compared to market approved DCB with 3.5 µg Ptx/mm².

Efficacy & Safety - 4 weeks
(in-stent stenosis)



Efficacy: clear tendency to **reduce in-stent neointima formation** and **LLL** vs. market approved DCB with 3.5 µg Ptx/mm². Safety: **no clinical or functional abnormalities** throughout the study up to 12 x 6 µg Ptx/mm² DEB per animal (e.g., weight gain, blood pressure, ECG, LVEF, hematology).

Gemeinhardt et al. Cardiovasc Intervent Radiol. 2022 Dec;45(12):1822-1831.

Clinical trial: MARATHON-SFA - 2026

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Safety and efficacy of double-dose DCB in treatment of complex superficial femoral artery lesions

Indication	DCB angioplasty for endovascular treatment of superficial femoral artery restenosis and in-stent restenosis
Study design	Randomised, controlled, multicenter trial, 2 groups (6 µg Ptx/mm^2 vs. regular dose Ptx-DCB, 1:1)
Safety endpoint (30 days)	Freedom from device- and procedure-related events (thrombosis, embolization, amputation, death, target lesion reintervention)
Efficacy endpoint	Primary patency at 24 months (FUP 6, 12, 24, 36 months)
Further safety endpoint	Major adverse events (target lesion reintervention, amputation, death) at 6, 12, 24 and 36 months
Sponsor	InnoRa GmbH