How do the VOYAGER PAD data help us understand the risks of Paclitaxel

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Disclosure

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I have the following potential conflicts of interest to report:

Grant support to CPC Clinical Research from Amgen, AstraZeneca, Bayer, Janssen, Merck, NovoNordisk
VOYAGER PAD

Trial Design
6,564 Patients with Symptomatic Lower Extremity PAD* Undergoing Peripheral Revascularization

ASA 100 daily for all Patients
Clopidogrel at Investigator’s Discretion

Randomized 1:1 Double Blind

Stratified by Revascularization Approach (Surgical or Endovascular) and Use of Clopidogrel

Follow up Q6 Months, Event Driven, Median f/u 28 Months

Primary Efficacy Endpoint: Acute limb ischemia, major amputation of vascular etiology, myocardial infarction, ischemic stroke or cardiovascular death

Principal Safety Endpoint: TIMI Major Bleeding

Primary Endpoint
Acute limb ischemia, major amputation for vascular cause, myocardial infarction, ischemic stroke, CV death

Cumulative Incidence (%)

Placebo
Rivaroxaban

HR 0.85
95% CI 0.76 – 0.96
P=0.0085

ARR, absolute risk reduction; NNT, number needed to treat

Bonaca MP, et al. NEJM 2020

An affiliate of:
Results

- Median follow-up of 31 months (IQR 25, 37 months)
- Complete ascertainment of vital status in 99.6% of patients

<table>
<thead>
<tr>
<th></th>
<th>Overall</th>
<th>No DCD</th>
<th>DCD</th>
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<tbody>
<tr>
<td>Proportion of patients</td>
<td>3888</td>
<td>2658</td>
<td>1230</td>
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| Drug-coated balloon | n=235 17% | n=70 5% | n=1053 78% |
| Drug-eluting stent  | n=1358 31% | n=3021 69% |

*1 patient missing lesion location
Inverse Probability Treatment Weighting
Standardized Differences

Unweighted

Weighted

Difference (Treated-Control)
All-cause Mortality

**Weighted**

N=4,316
n=394 deaths

Not drug-coated

Drug-coated

Cumulative Incidence (%)

Months from Randomization

HR 0.95
95% CI 0.83 – 1.09
P=0.49

Stabilized weights
HR 0.95
95% CI 0.77 – 1.18
P=0.66

Hess CN...Bonaca MP et al. TCT 2020
## Mortality and DCD Use by Device Type

*Weighted Hazard*

<table>
<thead>
<tr>
<th>Device Type</th>
<th>DCD n/N (%)</th>
<th>No DCD n/N (%)</th>
<th>HR (95% CI)</th>
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</thead>
<tbody>
<tr>
<td>DCB vs. PTA</td>
<td>61/820 (7.4)</td>
<td>144/1479 (9.7)</td>
<td>0.99 (0.82, 1.20)</td>
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<tr>
<td>DES vs. BMS</td>
<td>19/231 (8.2)</td>
<td>148/1495 (9.9)</td>
<td>1.04 (0.84, 1.28)</td>
</tr>
</tbody>
</table>

**Abbreviations:**
- DCB = drug-coated balloon
- PTA = percutaneous transluminal angioplasty
- DES = drug-eluting stent
- BMS = bare metal stent

**Note:** The chart shows the weighted hazard ratio for mortality comparing DCD (donor cardia death) to no DCD, with DCB (drug-coated balloon) vs. PTA (percutaneous transluminal angioplasty) and DES (drug-eluting stent) vs. BMS (bare metal stent) as device types.
Unplanned Index Limb Revascularization

Weighted

Cumulative Incidence (%)

Months from Randomization

21.5%

24.6%

HR 0.84

95% CI 0.76 – 0.92

P=0.0003

Drug-coated

Non drug-coated

N=4,059

3 Years

ARR 2.6%

NNT 39

24.6%

21.5%

6 mos

ARR 2.3%

NNT 44

HR 0.84

95% CI 0.76 – 0.92

P=0.0003

N=4,059

Hess CN…Bonaca MP et al. VIVA 2020
Summary and Conclusion

• In a large contemporary PAD trial with ~1400 receiving DCD and ~400 deaths there was no association between DCD and mortality

• DCD use was not associated with amputation risk or acute limb ischemia

• DCD use was associated with a 2.6% absolute reduction in the need for unplanned index limb revascularization (NTT 39) over 3 years from intervention