The Paclitaxel Controversy: Where Are We Now?

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Disclosure

Speaker name:
...........................................................................

I have the following potential conflicts of interest to report:

- [x] Consulting
- [ ] Employment in industry
- [ ] Stockholder of a healthcare company
- [ ] Owner of a healthcare company
- [ ] Other(s)

- [ ] I do not have any potential conflict of interest
What is Paclitaxel?

- Best known as a chemotherapeutic drug
- Interferes with microtubule formation during the cell cycle
- Causes cell death through apoptosis
- Physical properties make it easy to introduce into the arterial wall
Restricting the development of restenosis

Zilver PTX 2-year patency

IN.PACT DCB 2-year patency

Paclitaxel is effective in restricting restenosis

IN.PACT DCB 2-year CD-TLR
Restricting the development of restenosis

IN.PACT DCB 5yr CD-TLR

Calcium burden assessment and impact on drug-eluting balloons in PAD.¹

Katsanos Meta-Analysis

JAHA Meta-Analysis
Risk of death at 2 years

12 RCTs with 2,316 cases

Crude risk
7.2% vs 3.8%

Risk Ratio
1.68 (95%CI: 1.15–2.47)

Risk Difference
3.5% (95%CI: 1.7–5.3)

Number-Needed-to-Harm
29 patients (95%CI: 19–59)

Figure 3. Random effects forest plot of all-cause death at 4 to 5 years. Pooled point estimate was expressed as risk ratio (RR).
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FDA Recommendations

• Continue monitoring these patients.
• Discuss the risks and benefits of all available PAD treatment options with your patients. For many alternative options to paclitaxel coated devices provide a more favourable risk-benefit profile.
• For individual patients judged to be at particular high risk for restenosis and repeat intervention clinicians may determine that the benefits outweigh the risk of late mortality.
CIRSE position

• In the majority of patients undergoing lower limb recanalization therapies alternatives to drug eluting devices should be used.

• For some individual patients at particularly high risk for restenosis clinicians may decide that the benefits outweigh the risks.

• Full informed consent required.

• Patients that have already received paclitaxel eluting devices should be follow up.
BfArM position

• Undertake careful risk-benefit assessment
• Involve your patients in the decision. It should be pointed out in conversation and in the declaration of consent that there is an increased probability of death from 2 years after use of paclitaxel-coated balloons and stents than with uncoated products.
• In all cases, other than those at particularly high risk of restenosis, alternative treatment methods should preferably be considered.
• Patients who have been treated with a paclitaxel-coated stent or balloon should be carefully monitored over the long term and at regular intervals.
CMS Beneficiaries

MEDICARE BENEFICIARY DATA ANALYSIS: PAD SEVERITY - WEIGHTED RESULTS*
NO DIFFERENCE IN MORTALITY DESPITE DIFFERENCE IN SEVERITY

Non-CLI: 61.3% (N=93,432)

Non-CLI
Log-rank P<0.001
Adjusted HR 0.94; 95%CI 0.92, 0.96

CLI: 38.7% (N=59,041)

CLI
Log-rank P<0.001
Adjusted HR 0.94; 95%CI 0.92, 0.97

Cumulative Incidence of Death

Days from Index Procedure

Non-drug Drug
Non-drug Drug

60.1% 58.3%
BARMER German Health Insurance

64,771 patients

Freisinger, E. et al. Eu Heart J 2019
Figure 3. Forest plots of five year survival by treatment approach using propensity score matched cohorts with hazard ratios and 95% confidence intervals (balloon vs. stent vs. both approaches merged together). All analyses were stratified in (A) chronic limb threatening ischaemia and (B) intermittent claudication.
Where are we now?

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- 2 huge healthcare datasets
- 3 analyses
- No mortality signal
- 1 suggested benefit
- 1 based on initial therapy
- Older age group
- Not randomised
- Limited detail
- No cause of death

- 4 meta-analyses
- Well performed
- No dose relationship
- No credible causation
- Possible ascertainment bias
Katsanos BTK meta-analysis

- Early (1 year) reduced amputation free survival.
- Reduced TLR
- Suggests early amputation due to embolisation
Local Toxicity
Aneurysm Formation

Patient B

Aneurysm Formation

Patient A

Bisdas T, Eluvia Registry

8% aneurysms

3 years

6 months

7% aneurysms
SUMMARY

• There are conflicting lines of data regarding the effect of paclitaxel on late mortality.
• There is a new meta-analysis suggesting worse amputation free survival following the use of paclitaxel drug coated ballons to manage BTK disease in patients with predominantly CLI.
• Local toxicity requires further data.
Thank you