Bifurcations Have Met Their Match

PERSPECTIVES ON CLINICAL RESEARCH AND TREATMENT FROM AN INTERNATIONAL PANEL OF EXPERTS

Tryton Medical recently invited several leading interventional cardiologists to share their opinions about treatment of coronary bifurcations and their assessments of recent clinical data.

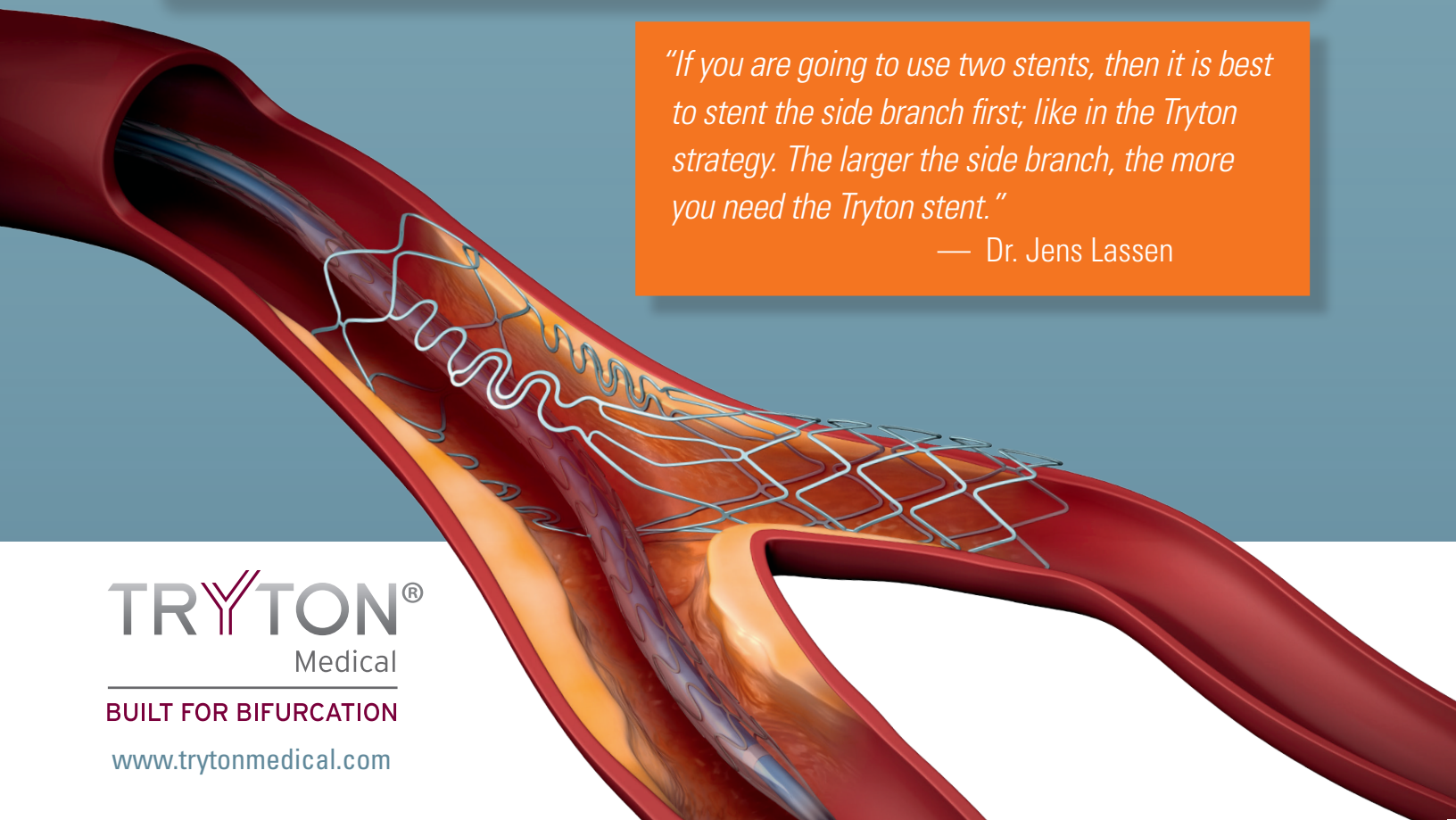
In a series of one-on-one discussions, these experts shared their perspectives on a range of topics including:

- Key factors that drive decisions in the use of provisional versus two-stent procedures, especially related to treatment in larger vessels (≥ 2.25 mm by QCA).
- Clinical data related to treatment of bifurcations, including the ESC and EBC guidelines, LEADERS trial and the Tryton IDE Randomized Clinical Trial.
- Use of Tryton Side Branch Stent compared to provisional strategy.
- Implications for left main interventions.

Investigational device in US and not approved for Japan.

"If you are going to use two stents, then it is best to stent the side branch first; like in the Tryton strategy. The larger the side branch, the more you need the Tryton stent."

— Dr. Jens Lassen



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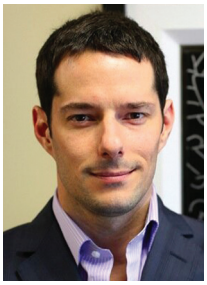
Introduction

11,000+ patients have now been treated with the Tryton Side Branch Stent, with clinical data collected in 1,800+ of these patients. Both the IDE pivotal study and the Extended Access Registry add to the body of clinical evidence supporting the use of Tryton Side Branch Stent in treatment involving ≥ 2.25 mm side branch vessels.

The board of experts who participated in this discussion included:

Prof. Adrian Banning
John Radcliffe Hospital
Oxford, United Kingdom



Dr. Philippe Généreux
Columbia University Medical Center
New York, NY, USA
Hôpital du Sacré-Coeur de Montréal
Montréal, QC, Canada

Dr. James Hermiller
St. Vincent Hospital / The Heart Center of Indiana
Indianapolis, IN, USA

Dr. Jens Lassen
Rigshospitalet University of Copenhagen
Copenhagen, Denmark

Dr. Maciej Lesiak
University Hospital
Poznan, Poland

Dr. Goran Stankovic
Clinical Center of Serbia
Belgrade, Serbia and Montenegro

Recent clinical research, including the LEADERS trial, has shown that about 20% of treated lesions occur at a bifurcation site.

- In many cases, experts conclude that the incidence of bifurcation may be higher than is generally estimated.
- The LEADERS trial reports that up to 75% of bifurcation lesions get a second wire to protect the side branch.

How often do you see patients with bifurcated lesions in your practice?

Dr. Lesiak:
I can agree that between 15 and 20 percent of patients have bifurcation lesions. As for double stent techniques, it may be 20% or maybe a little more in my center.

Dr. Généreux:
I think these results are very conservative. I think in practice it's maybe higher. When you talk about complex bifurcation and we are dealing with more and more diseased patients, older patients, I think it's maybe around 30-40%.

> In my practice at least a quarter of the patients, probably more, have bifurcations. And then at least 30 - 40% require a two-stent strategy.
>
> – Dr. James Hermiller

Experts agree that treatment of bifurcation lesions requires special considerations.

> In large vessel bifurcations especially, the assessment of angulations, plaque compositions, and the myocardium at risk, determine the most optimal treatment strategy tailored to the patient.

> With these factors in mind, experts find that current stents are often inadequate because they are intended specifically for straight vessels. The Tryton Side Branch Stent with Tri-ZONE® Technology is designed to provide complete lesion coverage accommodating all vessel types.

Dr. Lesiak:
Treating bifurcation lesions is generally a more difficult procedure, taking more time and needing more expertise.

Prof. Banning:
With 1,1,1 bifurcations with disease extending 6-7 mm within the side branch, treating with a provisional approach is going to be difficult, especially when stenosis is angulated and severe.

Dr. Hermiller:
The problem with bifurcations is our stents were made for straight tubes. They were not made for Ys and Ts. So the fundamental issue is we don't have the technology today, we have just an incredible number of workarounds.

Dr. Généreux:
The important thing is the complexity of the bifurcation. If it's a true bifurcation, with mainly the side branch diseased, is the first factor. Then the other major point is the size of the side branch – if it is a relevant side branch, meaning more than 2.25 mm (by QCA).

When considering a provisional versus two-stent strategy, there are many factors to consider:

> size of the side branch and myocardium at risk

> size of plaque burden and complexity of disease

> how complex is it to wire

Dr. Hermiller:
When it's truly complex, which generally means the side branch is involved, it's often two-stent.

Dr. Généreux:
I think provisional could be a good strategy when you deal with a small side branch, a small territory at risk, or non-significant lesions either visually assessed or by FFR, but this scenario does not occur that frequently.

Dr. Lassen:
The more the operator feels uncomfortable about losing the side branch, the more treatment of the side branch is paramount. If you are going to use two stents then it is best to stent the side branch first; like in the Tryton strategy. The larger the side branch, the more you need Tryton.

> If I see a large plaque burden within the side branch or very tight diffuse stenosis in the main vessel, side branch stenting is mandatory.
> – Dr. Maciej Lesiak

Treatment guidelines are helpful but should not be restrictive.

> Experts agree that established guidelines can help define an overall strategy to treat bifurcations, but these should not be applied unilaterally to every patient and every bifurcation lesion.

> There is strong support for the ability to use a tailored approach to ensure that patients are not treated with a provisional strategy when other options may be better.

Prof. Banning:
I think for smaller side branches the decision really about two stents is whether you are prepared to let it occlude (when treating provisional).

Dr. Généreux:
I think we need to assess the guidelines… personally, I think they are too limiting. We need to put some nuance. You cannot apply a global strategy to every single patient. Clearly some bifurcations up front will need a two-stent approach. And in some situations it could be dangerous and a risk to choose a provisional approach.

Rapidly expanding clinical data are changing the way we think about treatment of bifurcations. Tryton Real World Experience – Studies involving 1,800+ patients prove that Tryton Side Branch Stents match the unmet need for significant bifurcation lesions.

- In just the last few years the range of available clinical data in treatment of bifurcations has expanded dramatically, most notably through the Tryton IDE Data.
- Findings from the IDE data show that lesion, procedure, and device success is achieved more frequently in the bifurcation stent group compared with the provisional group.
- Clinicians report that they are better able to treat two-stent bifurcations using Tryton with predictable angiographic outcomes.

What procedural benefits do you see with Tryton versus provisional?

- Confidence and predictability in the procedure – it can be done quickly and accurately while maintaining control.
- Tryton is designed to provide complete lesion coverage and accommodate all vessel types.
- Effective and easy to use.

> I would say that the Tryton stent is easy to use, and is highly predictable and for any level of experience operator.
>
> – Dr. Philippe Généreux

Prof. Banning:

It should give you confidence that you can do this two-stent technique (Tryton in side branch and DES in main branch) accurately and quickly and that the stent deployment, particularly in the side branch, can be optimal once you complete it. It is likely that recrossing will not be complicated and that angiography or IVUS results will be good.

> This is the first bifurcation stent out there that I think has been effective and simple to use...you feel that you have control throughout the case.
>
> – Dr. James Hermiller

The IDE Study supports the use of Tryton stents in large bifurcations and vessels ≥ 2.25 mm.

- In the IDE study, the outcome was affected because 60% of vessels were smaller than 2.25 mm and therefore below the minimum expected vessel size.
- The Tryton IDE Study showed reductions in target vessel failure and statistical difference of side branch percent diameter stenosis in patients with side branch vessels of ≥ 2.25 mm (by QCA).

> I kind of expected this outcome when you use the enhanced culotte and secure the side branch first in adequately sized side branches you can expect the best outcome for Tryton compared to current standard provisional.
>
> – Dr. Goran Stankovic

Dr. Lassen:

The Tryton IDE study, like the Nordic 4 study, shows that as the diameter of the side branch increases the positive effect of having two stents is also increased.

Dr. Hermiller:

The 2.25 data look very encouraging for Tryton compared to provisional in what were really complex lesions. Not surprising at all that the larger sub-group with larger side branches look more effective in the Tryton cohort.

Dr. Lesiak:

If we follow the inclusion criteria precisely, the results would have been better. We have the answer in the secondary endpoint that the in-stent diameter stenosis in the side branch ostium was much better in the Tryton cohort, so it may translate with many patients into some clinical benefit.

> The results are encouraging within the patient population that the trial was set up to recruit. The safety data, especially in the larger vessels, is excellent.
>
> – Prof. Adrian Banning

Results of the Tryton IDE study and meta-analysis from studies like NORDIC-Baltic, BBC, and CACTUS confirm that the provisional strategy is preferred in smaller vessel populations.

Dr. Stankovic:
From NORDIC IV we learn there is big difference in outcome when the side branch is larger than 2.5 mm with 5-10 mm diffuse disease, it makes sense to start as intention to treat with two-stent strategy.

> They showed that with small side branches you should use provisional. I think the Tryton trial totally confirmed that and showed that we should treat large side branches and not treat small side branches.
> – Dr. Phillipe Généreux

Prof. Banning:
I think there is a risk that we swing and go too provisional, with people getting a bit lazy about putting that wire down. Ultimately you start to lose side branches and we make the technique more dangerous by trying to do too little.

Dr. Hermiller:
As we look at the meta-analysis of Nordic-Baltic, BBC, CACTUS studies, provisional strategy was favored over a two-stent strategy, not surprising at all. You end up with very small stents in those side branches, which leads to higher stent thrombosis rates. With the Tryton Stent, you're almost committed to an optimal implantation technique.

Post hoc analysis supports that Tryton stents work in large bifurcation lesions with SB ≥ 2.25 mm.

- Tryton can be used in a wide variety of angulations.
- It adjusts for the different vessels size geometries.
- Findings from the post hoc analysis from the IDE study could support revisions to prevailing guidelines related to treatment of significant and large side branches.
- Tryton as a BMS does not negatively influence the long-term result of the main vessel stenting.

> You need to select big enough vessels around 2.5 mm angiographically to create MACE with a provisional strategy. Those are actually the vessels and lesions to treat with Tryton where you can expect better outcomes as compared to provisional.
> – Dr. Goran Stankovic

Dr. Généreux:
Tryton is a very good option to keep the side branch open in all steps of the PCI. So I wish I could have access to the Tryton stent as soon as possible.

Dr. Hermiller:
When we look at the 2.25 data from the Tryton trial, it's not surprising at all that the percent diameter stenosis in the Tryton stent is superior to a provisional approach. You've got a side branch stent with Tryton that's really designed to provide maximal radial strength at the ostium where we see most of the late loss and reduced diameters in these side branches.

> This device is designed to treat side branches of 2.25 and larger. The post hoc analysis supports its use in these large bifurcations.
> – Dr. Maciej Lesiak

Dr. Généreux:
For me one of the reassuring things from the Tryton trial is that Tryton in the side branch did not affect the main branch outcomes.

Dr. Hermiller:
One of the advantages of the Tryton is that it can be used in a wide variety of geometries, including those with fairly straight up angulation and those with shallow angulation.

Dr. Généreux:
If you treat large side branch with Tryton stent compared to provisional, you will have benefit on the diameter of stenosis at follow up, patency of the vessel, and also on the primary endpoint which was target vessel failure. The data show Tryton is preferable in significant and large side branches, and this should influence clinical practice.

> Tryton is a valuable tool today, although it is not a drug eluting stent, it has repeatedly demonstrated in clinical studies that it is highly deliverable, safe, and effective. As the diameter increases the need for a drug eluting Tryton decreases.
> – Dr. Jens Lassen

Tryton has CE approval for use in left main.

> Tryton Side Branch Stents provide safe and predictable outcomes in the left main.

> It is designed for left main use providing ostial scaffolding at level of circumflex.

Dr. Lassen:
When dealing with the Left Main Coronary Artery, you need a quick and safe procedure. Intuitively, Tryton is the right thing to do. This stent is designed to accommodate both the left main and the side branch, thus providing optimal scaffolding in an easy to perform, predictable procedure.

Prof. Banning:
The challenge with bifurcations is around stent expansion, and the nice thing about the Tryton is the confidence you can have about the ostium of the circumflex, if the circumflex is the branch, when you've got good expansion.

Dr. Stankovic:
I do not feel uncomfortable using Tryton in 3.0 mm CX.

Dr. Hermiller:
We very often have to use a two-stent approach, particularly if there's plaque in that ostium. The preferred strategies depend a bit on how big the circumflex is compared to the left main and the LAD. If it's a big circumflex, then culotte works well. If it's a relatively small circumflex, then double-kiss crush or a tap is a bit better technique. Certainly the Tryton is ideal for this. You go ahead and safely get hold of the circumflex. You're not going to lose it, and you focus on the left main and LAD.

Dr. Lassen:
In the left main, Tryton may provide the optimal solution, your device is already tapered and it is designed to fit both the left main and the side branch.

> If I have a large circumflex – 3.0 mm for example – I protect and stent the left main LAD. Then the Tryton SHORT should fit in the majority of cases.
> – Dr. Maciej Lesiak

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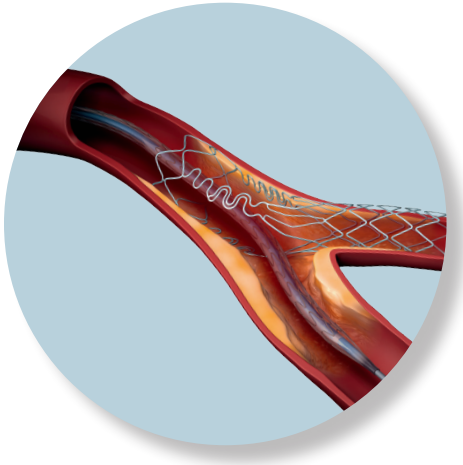

> Bifurcation disease is common in over 20% of PCI's.

> Extensive clinical data reinforces the benefits of Tryton stents in significant bifurcation lesions with side branches ≥ 2.25 mm.

> Tryton stents are designed to provide complete lesion coverage, while provisional stenting techniques are not.

> In the EU, clinicians find that Tryton stents provide safe and predictable outcomes in the left main.

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