The PROSPECT Trial

Providing Regional Observations to Study Predictors of Events in the Coronary Tree

A Natural History Study of Atherosclerosis Using Multimodality Intracoronary Imaging to Prospectively Identify Vulnerable Plaque

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PROSPECT Investigators
The PROSPECT Trial

700 pts with ACS
UA (with ECGΔ) or NSTEMI or STEMI >24º
undergoing PCI of 1 or 2 major coronary arteries
at up to 40 sites in the U.S. and Europe

PCI of culprit lesion(s)
Successful and uncomplicated
Formally enrolled

Metabolic S.
• Waist circum
• Fast lipids
• Fast glu
• HgbA1C
• Fast insulin
• Creatinine

Biomarkers
• Hs CRP
• IL-6
• sCD40L
• MPO
• TNFα
• MMP9
• Lp-PLA2
• others

PI: Gregg W. Stone
Sponsor: Abbott Vascular; Partner: Volcano
The **PROSPECT Trial**

3-vessel imaging post PCI

**Culprit artery, followed by non-culprit arteries**

Angiography (QCA of entire coronary tree)

**IVUS**

Virtual histology

Palpography (n=~350)

**Meds rec**

Aspirin
Plavix 1yr
Statin
Repeat biomarkers @ 30 days, 6 months

**F/U:** 1 mo, 6 mo, 1 yr, 2 yr, ±3-5 yrs

MSCT Substudy
N=50-100

Repeat imaging in pts with events

**Proximal 6-8 cm of each coronary artery**
Lesions are classified into 5 main types:

1. Fibrotic
2. Fibrocalcific
3. Pathological intimal thickening (PIT)
4. Thick cap fibroatheroma (ThCFA)
5. VH-thin cap fibroatheroma (VH-TCFA) (presumed high risk)
PROSPECT: Primary Endpoint

MACE attributable to rapid angiographic progression of a non-culprit lesion*

- Cardiac death
- Cardiac arrest
- Myocardial infarction
- Unstable angina
  - Requiring revascularization
  - Requiring rehospitalization
- Increasing angina
  - Requiring revascularization
  - Requiring rehospitalization

MACE during FU were adjudicated by the CEC as attributable to culprit lesions (those treated during or before the index hospitalization) or non culprit lesions (untreated areas of the coronary tree) based on angiography (+ECGs, etc.) at the time of the event; events occurring in pts without angiographic follow-up were considered indeterminate in origin. Rapid lesion progression = ↑ in QCA DS by >20% from baseline to FU.
**PROSPECT: MACE**

- **MACE (%)**
  - **Time in Years**
  - **0**
    - **All**
      - **Culprit lesion (CL) related**
      - **Non culprit lesion (NCL) related**
      - **Indeterminate**
      - **Number at risk**
        - **ALL** 697
        - **CL related** 697
        - **NCL related** 697
        - **Indeterminate** 697
  - **1**
    - **13.2%**
    - **7.9%**
    - **6.4%**
    - **1.9%**
  - **2**
    - **18.1%**
    - **11.4%**
    - **9.4%**
    - **2.7%**
  - **3**
    - **20.4%**
    - **12.9%**
    - **11.6%**
    - **2.7%**

**Number at risk**
- **ALL** 697
- **CL related** 697
- **NCL related** 697
- **Indeterminate** 697

**In the diagram:**
- Red line: All
- Blue line: Culprit lesion (CL) related
- Yellow line: Non culprit lesion (NCL) related
- Green line: Indeterminate

**Graph description:**
- The graph shows the percentage of major adverse cardiovascular events (MACE) over time, categorized by different lesion-related causes.
**PROSPECT: NCL MACE**

- Non-culprit lesion (NCL) related, all
  - Without rapid lesion progression (RLP)
  - With rapid lesion progression (RLP)

**Median time to event**
- No RLP: 223 [85, 663] days
- RLP: 401 [229, 666] days

**Number at risk**
- NCL related, all: 697 595 553 521
- Without RLP: 697 610 577 551
- With RLP: 697 620 579 550
**PROSPECT: Correlates of Non Culprit Lesion Related Events**

**Lesion HR**

<table>
<thead>
<tr>
<th>Lesion</th>
<th>HR (95% CI)</th>
<th>P value</th>
<th>Prevalence*</th>
</tr>
</thead>
<tbody>
<tr>
<td>TCFA</td>
<td>3.8 (2.2, 6.6)</td>
<td>&lt;0.0001</td>
<td>51.2%</td>
</tr>
<tr>
<td>MLA ≤4.0mm²</td>
<td>5.0 (2.9, 8.7)</td>
<td>&lt;0.0001</td>
<td>49.1%</td>
</tr>
<tr>
<td>PB ≥70%</td>
<td>7.9 (4.6, 13.8)</td>
<td>&lt;0.0001</td>
<td>30.7%</td>
</tr>
<tr>
<td>MLA ≤4mm² + TCFA</td>
<td>6.4 (3.4, 12.2)</td>
<td>&lt;0.0001</td>
<td>17.4%</td>
</tr>
<tr>
<td>PB ≥70% + MLA ≤4mm²</td>
<td>6.7 (3.4, 13.0)</td>
<td>&lt;0.0001</td>
<td>15.4%</td>
</tr>
<tr>
<td>PB ≥70% + TCFA</td>
<td>10.8 (5.5, 21.0)</td>
<td>&lt;0.0001</td>
<td>11.0%</td>
</tr>
<tr>
<td>PB ≥70% + MLA ≤4mm² + TCFA</td>
<td>10.8 (4.3, 27.2)</td>
<td>&lt;0.0001</td>
<td>4.6%</td>
</tr>
</tbody>
</table>

*Likelihood of one or more such lesions being present per patient. PB = plaque burden at the MLA*
• From this trial, the first prospective, natural history study of atherosclerosis using multimodality imaging to characterize the coronary tree, we can conclude that:

  • Approximately 20% of pts with ACS successfully treated with stents and contemporary medical Rx develop MACE within 3 years, with adverse events equally attributable to recurrence at originally treated culprit lesions (treatment failure) and to previously untreated non culprit coronary segments

  • Approximately 12% of pts develop MACE from non culprit lesions during 3 years of follow-up

  • Patients treated with contemporary medical therapy who develop non culprit lesion events present most commonly with progressive or unstable angina, and rarely with cardiac death, cardiac arrest or MI
• While plaques which are responsible for unanticipated future MACE are frequently angiographically mild, most untreated plaques which become symptomatic have a large plaque burden and a small lumen area (which are detectable by IVUS but not by angiography).

• Only about half of new events due to non culprit lesions exemplify the classic notion of vulnerable plaque (rapid lesion progression of mild angiographic lesions), while half are attributable to unrecognized and untreated severe disease with minimal change over time.

• The prospective identification of non culprit lesions prone to develop MACE within 3 years can be enhanced by characterization of underlying plaque morphology with virtual histology, with VH-TCFAs representing the highest risk lesion type.

• The combination of large plaque burden (IVUS) and a large necrotic core without a visible cap (VH-TCFA) identifies lesions which are at especially high risk for future adverse cardiovascular events.