Clinical Trials in Peripheral Vascular Disease: Pipeline and Trial Designs—An Evaluation of ClinicalTrials.gov Data

Samantha Subnawal, MD, MA1, Maxwell R. Patel, MD, MD2, Hong Chen, PhD3, Bett H. Lillemoe4, William S. Jones, MD5, Michael S. Creme6, MD7, Christopher J. White8, MD9, William R. Haefl10, John R. Landon11, MD11, Robert H. Carll1213
1. Duke University School of Medicine, Durham, NC; 2. MD State University, Bangor, ME; 3. US Veterans Health Administration, Oxnard, CA; 4. Duke Heart and Vascular Institute, New Orleans, LA; 5. University of Colorado, Aurora, CO; 6. University of California Davis, Sacramento, CA

Methods

- An initial subset of 3,375 studies with at least one CONDITION or CONDITION_BROWSE term potentially relevant to PVD were identified and manually reviewed (SS, WSU).
- Studies of external invalidating devices, management of sequence of vascular disease (in the rehabilitation or atherosclerosis), brain In A-V malformations, orthostatic hypotension, weekend, and chronic cephalothin were insufficiently excluded.
- Each study was categorized as arterial vs. valvular trials. Primary and secondary prevention of vascular events were included if there was specific inclusion of patients with history of stroke, cardiac disease, or lower extremity peripheral artery disease (PAD).
- Studies enrolling patients with extracardiac vascular disease with the endpoints looking at plaque regression, plaque stability, increase in inflammatory biomarkers, improvements in endothelial function, and measurements of arterial medial thickness were categorized as prevention studies.
- Studies of arterial stent trials were categorized under valvular disease.
- Studies including cardiac conditions were identified by cardiologist specialties at Duke Clinical Research Institute. PIVD studies were excluded from this group which was used as a comparison group.
- Studies were allowed to be in more than one subgroup if they enrolled patients categorized within different subgroups.
- Within the United States, we described regional access to PIVD clinical trials graphically on a map at the zip code level

Results

- A dataset of 96,345 clinical trials in CTTI were downloaded in XML format in October 2010, and captured in a database for aggregate analysis.
- Analysis was restricted to 40,970 “interventional” study trials. Analysis was limited to those trials of extracardiac vascular disease (arterial or venous) have provided greater options for treatment of the underlying disease.

Conclusions

- Despite the IOM’s priority to perform comparative effectiveness trials in arterial disease, a majority of the clinical trials did not include an active comparator: therefore changes are needed to reduce barriers to perform trials with active comparators, or alternatively, other methods are necessary to compare therapies beyond randomized trials.
- PIVD trials investigate a greater percentage of drug and device therapies than cardiology trials, and are more likely have industry as lead sponsor and funding source.
- There is wide heterogeneity in interpretation of the data fields by those entering responses into CTG.

Disclosures:

- KC: None
- MG: Johnson and Johnson, Pfizer, Bayer, OrthoMcNeil Jansen
- MG: Merck, AstraZeneca, Baxter, Genzyme, Janssen, St. Jude and Baxter
- BR: Medtronic, CoreValve
- BR: AstraZeneca, Baxter, Genzyme, Johnson & Johnson, Pleuristem, Astra Zeneca, Neovasc; St. Jude and Baxter
- KC: shareholder; Abbott vascular, Boston Scientific, Bard Peripheral Vascular, Medtronic
- NI: Consultant/advisory board member: Abbott vascular, Bard peripheral vascular, medtronic
- NI: A list of all acknowledged individuals is available at www.washington.edu
- Financial support for this project was provided by grant UI1RR0128001 from the U.S. Food and Drug Administration awarded to Duke University for the Clinical Trials Transformation Initiative.

Contact

Samantha Subnawal, MD, MBA
samantha.subnawal@duke.edu
Duke Clinical Research Institute
Duke University
Durham, NC

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Background

- Recent advances in therapies of peripheral vascular disease (arterial or venous) have provided greater options for treatment of the underlying disease.
- The IOM is a top priority topics for comparative effectiveness research lists peripheral artery disease as one of only two cardiovascular conditions in the top 20.
- Little is known about the current state of the entire peripheral vascular disease (PVD) trial portfolio and current trial designs.
- The ClinicalTrials.gov (CTG) registry comprises over 200,000 trials in 175 countries, and is the most utilized public source for clinical trial information worldwide.
- The Clinical Trials Transformation Initiative (CTTI) is a public-private partnership founded by the U.S. Food and Drug Administration and Duke University, and includes more than 50 organizations across the clinical trial enterprise, with the goal to identify the quality and efficiency of clinical trials and generate evidence about how to improve the design and execution of clinical trials.

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Consequently, using the CTTI database of trials registered in the CTG, we sought to describe the current state of clinical trials for treatment of PVD

Methods

- Analysis was limited to those trials of extracardiac vascular disease (arterial or venous) have provided greater options for treatment of the underlying disease.
- Studies of external invalidating devices, management of sequence of vascular disease (in the rehabilitation or atherosclerosis), brain In A-V malformations, orthostatic hypotension, weekend, and chronic cephalothin were insufficiently excluded.
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- Within the United States, we described regional access to PIVD clinical trials graphically on a map at the zip code level

Table 1: Overall study characteristics

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<th>Characteristic</th>
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<th>2008</th>
<th>2009</th>
<th>2010</th>
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<td>Sites in US (%)</td>
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<td>29.3</td>
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<td>37.5</td>
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<tr>
<td>Sites in other (%)</td>
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<td>62.5</td>
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<td>62.5</td>
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<tr>
<td>Total Intermittent Critical Limb</td>
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<td>189</td>
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<tr>
<td>Acute Limb Ischemia</td>
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<td>230</td>
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<tr>
<td>Arterial Ulceration</td>
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<td>199</td>
<td>189</td>
<td>230</td>
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</tbody>
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Figure 1: Breakdown of arterial and venous trials in ClinicalTrials.gov

Table 2: Subgroups of arterial trials

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Figure 2: Breakdown of arterial and venous trials in ClinicalTrials.gov

Figure 3: Breakdown of venous trials

Figure 4: Breakdown of Aortic Disease Trials

Figure 5: Breakdown of Lower Extremity PAD Trials

Figure 6: Temporal Trend of PVD Trials

Figure 7: Geographic distribution of PIVD studies by zip code within the continental United States. Size and color of dot represents number of PIVD trials with a site at each zip code location.

Limitations

- There is wide heterogeneity in interpretation of the data fields by those entering responses into CTG.
- The data were not independently verified in this analysis.

Conclusions

- Despite the IOM’s priority to perform comparative effectiveness trials in arterial disease, a majority of the clinical trials did not include an active comparator: therefore changes are needed to reduce barriers to perform trials with active comparators, or alternatively, other methods are necessary to compare therapies beyond randomized trials.
- PIVD trials investigate a greater percentage of drug and device therapies than cardiology trials, and are more likely have industry as lead sponsor and funding source.
- Because the PIVD field is underinvestigated in clinical trials, despite data demonstrating benefit of exercise therapy in these patients.
- >50% of trials enroll patients from outside of U.S.; there is a trend of increasing enrollment outside of the U.S.
- There is geographic variation in access to clinical trials with populations in the midwest and west having limited geographic access to these trials despite it being known these locations have higher incidence of arterial disease.