Vascular endothelial growth factor A (VEGF-A) (AZD-8601)

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Vascular endothelial growth factor (VEGF-A) overview

- VEGF-A is a potent angiogenic factor that promotes growth of blood vessels.
- Preclinical data suggests that expression of this growth factor in the ischemic heart could increase blood flow and partially restore cardiac function.
- Coronary artery disease, the primary cause of ischemic heart failure, affects the arteries providing blood supply to the cardiac muscle.
- In 2015, coronary artery disease resulted in 366,000 deaths in the United States, and 8.9 million deaths globally.
VEGF-A (AZD8601)

Phase 1 successful, Phase 2 ongoing

**Phase 1**

- Intradermal injection, mRNA vs. placebo, in diabetic patients

**Phase 2**

- Intracardiac injection, mRNA vs. placebo, in patients undergoing CABG
VEGF-A (AZD8601)
Phase 1 first-in-human study demonstrated safety and tolerability

Safety and tolerability monitoring procedure:
- Adverse events were monitored from screening and during the 6-month follow-up period
- Vital signs (pulse and blood pressure), electrocardiography, physical examinations, and laboratory assessments (hematology, blood biochemistry, coagulation, urinalysis, viral serology, and urine drug and alcohol tests)
- Local reactions at injection sites: redness, bruising, swelling, itching and pain

Safety results and conclusions:
- No adverse events leading to discontinuation occurred
- The only causally treatment-related adverse events were injection-site reactions (all mild), occurring in all but one participant receiving VEGF-A mRNA. These local reactions were attributable to VEGF-A-mediated vasodilation, supporting further clinical investigation of VEGF-A mRNA as an angiogenic therapy
- Minor changes from baseline in laboratory parameters or vital signs were noted but none of these was considered clinically relevant
VEGF-A (AZD8601) Phase 1a data

Intradermal AZD8601 gives rise to dose-dependent production of VEGF-A protein

Phase 1a microdialysis sampling of VEGF-A protein in diabetic patients

Proof of mechanism fulfilled following a single intradermal injection of AZD8601

Intradermal delivery of modified mRNA encoding VEGF-A in patients with type 2 diabetes

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VEGF-A (AZD8601) Phase 1b data

Single dose of intradermal VEGF-A mRNA acutely restored baseline skin blood flow

Phase 1b laser scanning microscopy of injection sites in diabetic patients

Acute improvement in skin blood flow

Intradermal delivery of modified mRNA encoding VEGF-A in patients with type 2 diabetes

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VEGF-A (AZD8601) Phase 2a to evaluate safety and activity on blood flow in a heterogeneous CABG population

**Injection sites in areas with impaired blood flow**
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