Patient and Physician Perspectives on Administration of the PCSK9 Monoclonal Antibody Alirocumab, an Injectable Medication to Lower LDL-C Levels

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This study was funded by Sanofi and Regeneron Pharmaceuticals
## Industry Relationships and Institutional Affiliations

<table>
<thead>
<tr>
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<th>Disclosure</th>
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<tbody>
<tr>
<td>Bertrand Cariou</td>
<td>Has received research funds from Sanofi and has received fees from consulting and/or advisory boards from Amgen, AstraZeneca, DebioPharm, Janssen, Eli Lilly, Genfit, Novo-Nordisk, Regeneron and Sanofi.</td>
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Alirocumab is a fully human monoclonal antibody which binds to and inhibits proprotein convertase subtilisin/kexin type 9 (PCSK9)

- Alirocumab (monotherapy or with background statin ± other lipid-lowering therapies) reduced LDL-C by 47.2–61.0% from baseline after 24 weeks of treatment in Phase 3 trials

Alirocumab 75 mg and 150 mg doses are each administered via 1 mL subcutaneous injection

However, many patients requiring lipid-lowering therapy will not have experience with injectable medications

Two delivery devices have been used in alirocumab clinical trials

- Pre-filled syringe
- Pre-filled pen

This study was designed to assess patient and physician perceptions of the usability and acceptance of these devices

- 400 participants (200 physicians and 200 patients) from US, France, UK, Germany, Italy, Spain
- Data collected via self-administered questionnaire
## Physicians

<table>
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<tr>
<th>Physicians (N=200)</th>
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<tbody>
<tr>
<td>Primary Care Physicians (PCPs)</td>
<td>99</td>
</tr>
<tr>
<td>Specialists (Cardiologists, Endocrinologists, Diabetologists, Lipidologists, Nephrologists [Germany only], Chemical pathologists [UK only])</td>
<td>101</td>
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<tr>
<td>Mean practice experience</td>
<td>17.8 yrs since residency</td>
</tr>
<tr>
<td>Average number of hypercholesterolemic patients</td>
<td>797</td>
</tr>
<tr>
<td>% patients receiving LLT</td>
<td>76.7%</td>
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- None of the physicians were investigators in alirocumab trials

LLT, lipid-lowering therapy.
Patients

- Patients were not at their LDL-C goal and had at least one of the following:
  - Familial hypercholesterolemia
  - Statin intolerance*
  - High cardiovascular (CV) risk**
  - Diabetes

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<tr>
<th>Patients (N=200)</th>
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<tbody>
<tr>
<td>Mean age</td>
<td>59.5 yrs</td>
</tr>
<tr>
<td>% Females</td>
<td>52%</td>
</tr>
<tr>
<td>% With experience of injectable medication (any medication)</td>
<td>25.5%</td>
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*Discontinued two or more statins due to muscle related side effects. Not currently receiving high dose statins. Not diagnosed with FH.

**Diagnosed with or experienced at least one CV event OR diagnosed with diabetes and at least 2 additional CV risk factors. Not diagnosed with FH or statin intolerant.
*Alirocumab identity was blinded, with an unbranded name (‘Voypaz’) used instead.

**Placebo was developed to mimic consistency and viscosity of active dose. Both doses used a 1 mL injection volume. Doses were tested in a randomly determined order.
After testing, participants responded to a list of statements about ease of use of the devices.

- Overall, positive responses related to usability.
- The majority of participants (83–100%) agreed with the statements.

Example statements included:

- *The injection is easy for patients to learn*
- *I would recommend the pen to my patients*
- *The pen is convenient to use, which can make it easy for you to stay with your treatment*
- *Visual and audio cues confirm when the injection begins and the injection is completed*
After testing, physician estimates of the % of their patients who would be willing to self-inject with the devices increased.

- **Pen (n=100)**: Pre 54, Post 66
  - Relative increase: 22%*
- **Syringe (n=100)**: Pre 50, Post 58
  - Relative increase: 16%*

*P<0.05, after testing vs. before testing
Physician Estimates of Patient Willingness to Self-Inject: PCPs vs. Specialists (Pen)

- Specialist estimates were higher than PCP estimates

**Bar Chart**
- **PCP**
  - Pre: 47%
  - Post: 61%
- **Specialist**
  - Pre: 60%
  - Post: 72%

Both P < 0.05 vs. PCP

**Notes**
- Pen (n=50)
- Pen (n=51)
Physician Estimates of Patient Willingness to Self-Inject: PCPs vs. Specialists (Syringe)

- Specialist estimates were higher than PCP estimates

**PCP**

- **Pre:** 43%
- **Post:** 53%

**Specialist**

- **Pre:** 57%
- **Post:** 63%

Both P<0.05 vs. PCP
Patients Reporting They Would Be "Very Willing" to Self-Inject According to Device

- The proportion of patients who reported they would be "very willing" to self-inject increased after testing.

![Bar chart showing the proportion of patients (%) who were "very willing" to self-inject before and after testing for Pen (n=100) and Syringe (n=100).](chart)

- Pen (n=100)
  - Pre: 57%
  - Post: 72%
  - Relative increase: 22%*

- Syringe (n=100)
  - Pre: 57%
  - Post: 63%
  - Relative increase: 11%

*P<0.05, after testing vs. before testing
After testing, the majority of patients indicated that they would be confident with self-injecting at home.
Those ≥60 vs. <60 Years Reporting They Would Be “Very Willing” to Self-Inject

There was a numerical but not statistical difference between responses for those ≥60 vs. <60 years.

*P<0.05; relative increase of 35% vs. pre-testing
Initially, patients with previous injectable medication experience were more willing to use the pen vs. injection-naïve patients; after testing there was no difference between groups.

- *P<0.05; relative increases of 38% (pen) and 14% (syringe) vs. pre-testing
Doses and Region

- **Doses**: No significant differences were observed in participant responses between the 75 mg and 150 mg doses.

- **Region**:
  - There were no significant differences between responses of physicians based in the US vs. the EU.
  - A greater proportion of patients in the US (82%) stated they would be very willing to self-inject with the pre-filled pen after testing compared with those from the EU (62%) (p<0.05).
    - No regional differences were found when using the pre-filled syringe.
Self-injection with alirocumab pre-filled pen and syringe devices was well accepted.

Devices were considered easy to operate, particularly after demonstration and testing.
- Willingness to use the pen device was slightly higher than the syringe.

Results suggest that in clinical practice, administration of alirocumab by either pre-filled pen or syringe would be acceptable for the majority of patients and physicians.