Diabetes therapy of tomorrow: Beyond glycemic control

IMI JDRF Joint Symposium, Bruxelles, Belgium

May 20th 2014

Philip J Larsen, Sanofi Diabetes
Prevalence of Diabetes by IDF Region

International Diabetes Federation, 2013 http://www.idf.org/diabetesatlas
Diabetes comes in two major flavors with plenty of nuances

- **Type 1 diabetes** (autoimmune disorder)
  - Latent autoimmune diabetes of the adult (LADA) could be considered etiologically and therapeutically categorized as T1DM variant

- **Type 2 diabetes** (heterogeneous disease with strong heritability)
  - Characterized by insulin resistance and impaired insulin secretion
  - Often macrovascular disease at time of diagnosis
But a person living with diabetes may find this classification of lesser relevance

54 years

Male, 83 - 85 kgs
Overweight,
Blue collar laborer,
No time for exercise

BMI > 25 kg/m²

HbA₁c 8%²

Is not only worried about his HbA1c

Cost¹

Diminishment of Self
Guilty, social stigma...

Lack of energy, irritability, erectile dysfunction

Blood pressure, Lipid, depression, CV issues

Underestimate the risk of complications

...failure, self blame, alone

HCP threat, Bad connotation, Amputation ...

Hypoglycemia, Titration, fear of Mistake

... don’t see the short term benefit

You don’t cope with the disease ruling, your existence you want to live a normal life²

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Diabetes double the risk of dying compared to anyone at the same age\textsuperscript{1}...

...Your physician will tell you to decrease your HbA1C\textsuperscript{2}

- 2 to 4 times higher risk for stroke
- 2 to 4 times higher risk for heart disease death
- 10 times more lower limb amputations
- Risk of blindness and kidney failure
- > 50\% chance of dying from CV disease

Each 1\% decrease in blood glucose levels reduces the risk of complications from diabetes (UKPDS)\textsuperscript{1}

- ↓14\% All-cause mortality
- ↓14\% Risk of myocardial infarction
- ↓21\% Risk of diabetes-related deaths
- ↓37\% Risk of microvascular complications
- ↓43\% Risk of amputation or PVD death

1. Risk of death among people with diabetes is twice that of people of a similar age without diabetes (1) 5 Million deaths WW
Diabetes care should not focus only on hyperglycemia
Complications are frequent

<table>
<thead>
<tr>
<th>Complication</th>
<th>T1 (%)</th>
<th>T2 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cholesterol</td>
<td>34</td>
<td>52</td>
</tr>
<tr>
<td>Depression</td>
<td>17</td>
<td>21</td>
</tr>
<tr>
<td>Heart / Circulation</td>
<td>14</td>
<td>22</td>
</tr>
<tr>
<td>Eyes (diabetes related)</td>
<td>13</td>
<td>12</td>
</tr>
<tr>
<td>Kidneys</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>Nerve damage</td>
<td>8</td>
<td>11</td>
</tr>
<tr>
<td>Feet</td>
<td>7</td>
<td>11</td>
</tr>
<tr>
<td>Other</td>
<td>12</td>
<td>12</td>
</tr>
</tbody>
</table>

H400 Some people may experience other health complications while they are managing their diabetes. Please tell us if you are currently undergoing treatment or taking medications for any of the following.

*Base: respondents with type 1 (n=1,073), respondents with type 2 (n=3,504)*
**THE PHYSICIAN- & PATIENT-ARCHETYPES**

### Physician

8 Patient-Archetypes

- **Type 1 and ½ diabetes**
  - 23%
- **Age-related diabetes**
  - 21%
- **Compliant patients with fast evolving diabetes**
  - 15%
- **Excel type**
  - 11%
- **Multi-morbid, very old**
  - 5%
- **Obese negligent**
  - 11%
- **Young obese**
  - 11%
- **Patients in “transition to insulin” – rejecting insulin injections**
  - 4%

**Base= Overall (n=1856)**

### Patient

3 Patient-Archetypes

- **Scared, worried & desperate**
  - 66%
- **Confused & Concerned with their treatment**
  - 25%
- **Proactive & confident**
  - 9%

**Base= Overall (n=864)**

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*T2D patients profiling, A+A, 2013, Base= Overall (n=1856)*

*SANOFI AVENTIS Diabetic Patients GALLILEO panel, November 2010, Base= Overall (n=864)*
Diabetes pharmacotherapy is a stepwise approach and falls in three categories:

- **Glucose RIGHT**
  - Insulins (various modalities)
  - Non-insulin super efficacious drugs
  - Devices
  - Adherence improvers

- **Glucose PLUS**
  - Weight management
  - Macrovascular disease modification
    - BP, lipids, inflammation
  - Complications management (e.g., renal)

- **Disease modification**
  - Insulin sensitization, β cell regeneration, anti-inflammatory

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**A**

**B**

**C**
R&D efforts: Prevention and Cure is the ultimate goal but several short-term achievable goals will help ease the disease burden.

- **IMI2 Innovation Network**
  - >10 years

- **Prevention and Cure Disease Modifying Therapy**
  - 5-10 years

- **Glucose Plus Towards individualized therapy**
  - 5-10 years

- **Focus on disease heterogeneity, comorbidities and late diabetic complications**
  - 5-10 years

- **Develop glucose controlling agents with Sustainable efficacy and additional CV benefits**
  - Today

- **Improve patients outcomes optimizing current therapies and**

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**Glucose Plus Diabetes R&D**

**Glucose Right Maximizing current drug based solutions**
The most important decision to make
Choice of target & link to disease segment

**High Confidence**

- Human Pharmacological Evidence
- Human Genetics or translational animal model

**Low Confidence**

- Mechanistic rationale or unproven animal model

Truly innovative, GLP1 agonism example hereof

Must increase focus in this tier - PCSK9 the prototype

Unfortunately, the majority of the industry discovery portfolio is in this tier. Aim should be to improve translatability or deprioritize the effort
Thank you