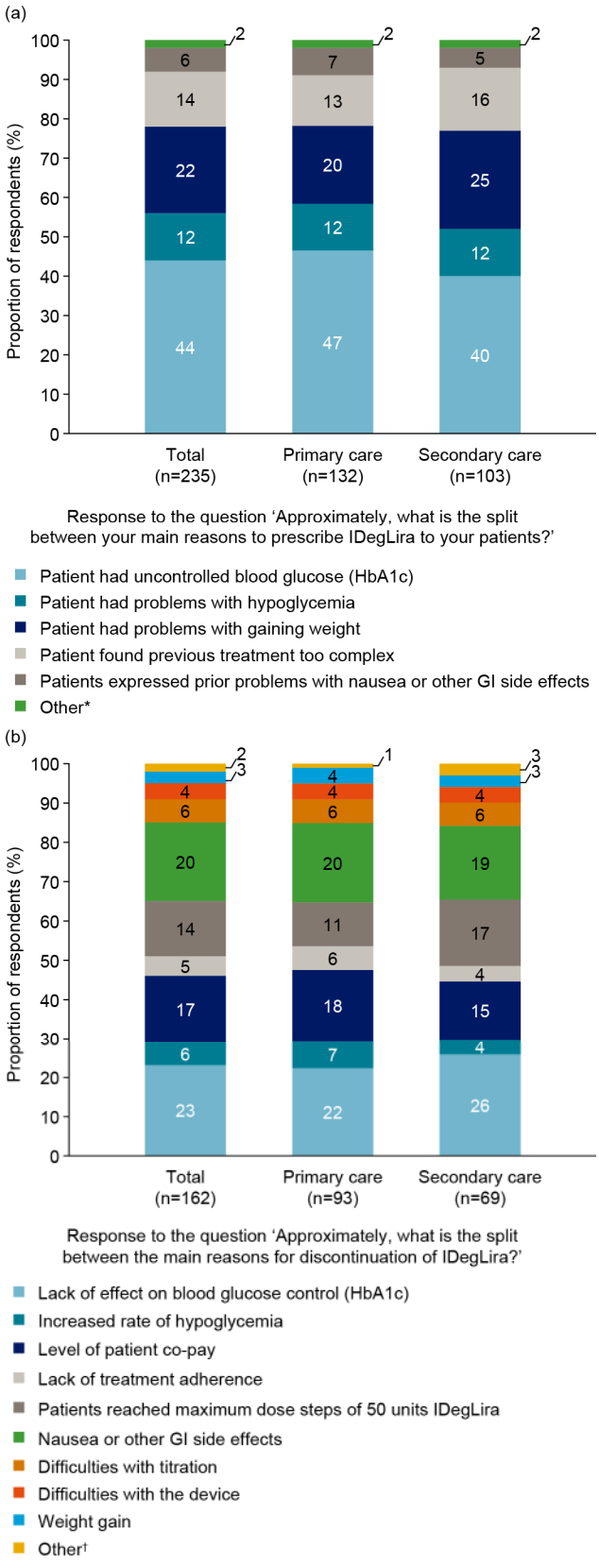
Supplementary material

Physicians' real-world experience with IDegLira: Results of a European Survey

Russell Drummond, Ankita Baru, Marcelina Dutkiewicz, Amaury Basse, Bengt-Olov Tengmark

Supplementary Figure 1: Main reasons for (a) initiating and (b) discontinuing IDegLira treatment in respondents' total IDegLira-treated patient population.

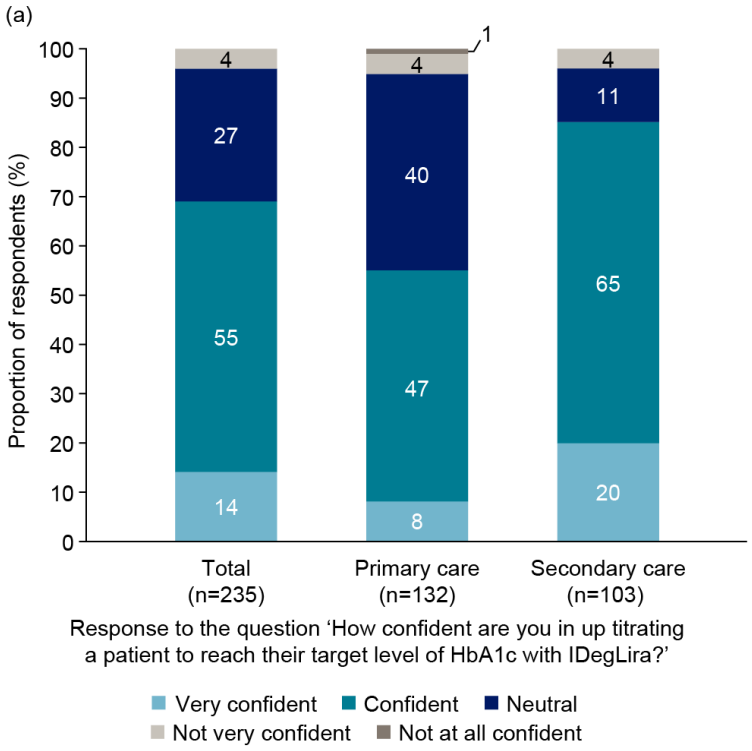


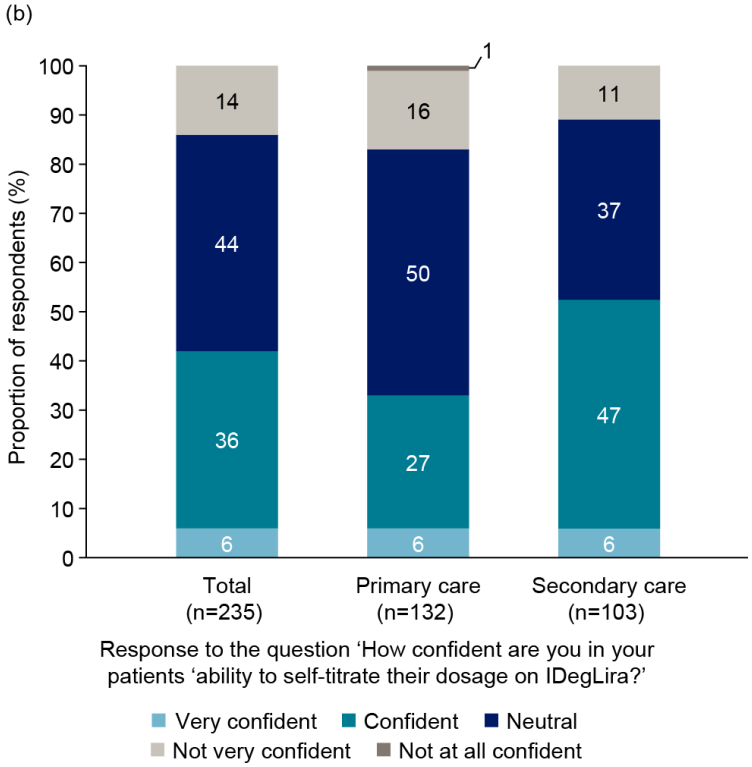
*Others include “Compliance, “Patient’s intolerability to previous treatment”, “Easy to use”, “Contraindications – SGLT-2/Renal insufficiency”, “Unable to achieve disease control with previous treatment”, “Patient’s lifestyle”, “Patient’s wish”, “Efficacy” and “Cost”.

†Others include “Lack of treatment adherence”, “Comorbidities – dementia, psychiatric”, “Dosage”, “Needle phobia” and “Don’t know/recall”.

GI, gastrointestinal; HbA1c, glycated hemoglobin; IDegLira, insulin degludec/liraglutide; SGLT-2, sodium/glucose cotransporter 2

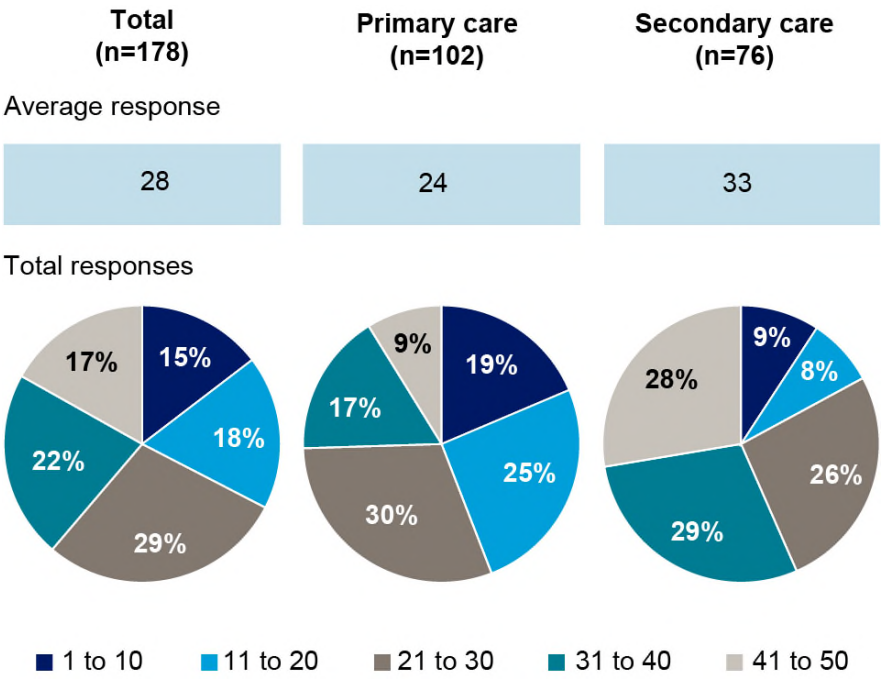
Supplementary Figure 2: Physicians' confidence in (a) up-titrating IDegLira; and (b) patient's ability to self-titrate with IDegLira.



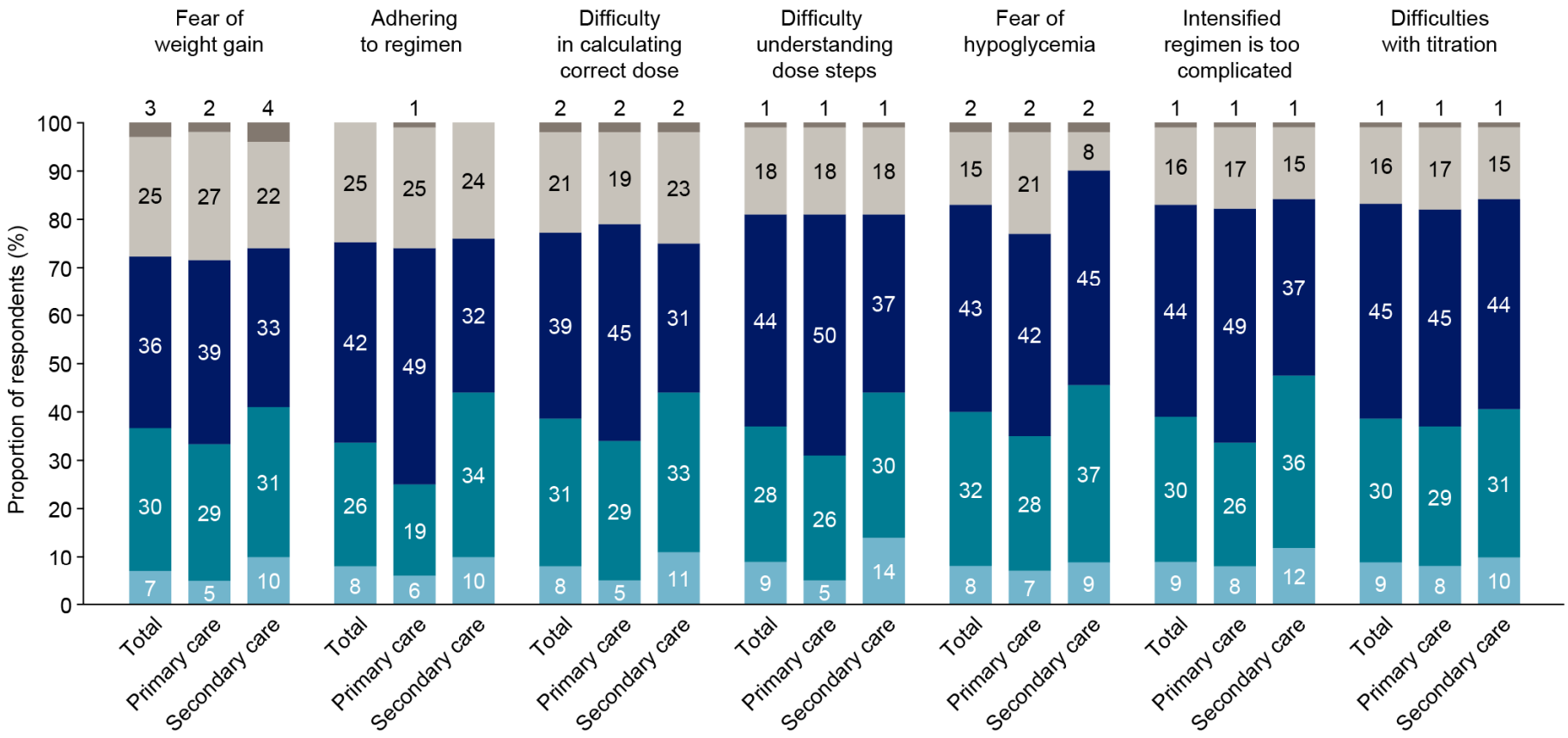


IDegLira, insulin degludec/liraglutide

Supplementary Figure 3 Daily dose of IDegLira (dose steps) in an average patient when they were in glycemic control



Supplementary Figure 4: Main patient concerns with IDegLira as reported by physicians



Response to the question 'Thinking about concerns expressed by all of your patients treated with IDegLira, how often are the following mentioned by your patients?'

IDegLira, insulin degludec/liraglutide

Questionnaire

AE REPORTING STATEMENT

We are required to pass on details of adverse events, product complaints, pregnancies or other safety information that are reported during the course of this survey to the sponsor of this market research.
Although what you say will, of course, be treated in confidence, should you raise during the discussion an adverse event, product complaint, pregnancy or other safety information, we will need to report this even if it has already been reported by you directly to the company or the regulatory authorities [for UK only: using the MHRA's 'Yellow Card' system]. In such a situation we need to know whether or not you are willing to waive the confidentiality given to you under the Market Research Codes of conduct specifically in relation to that adverse event, product complaint, pregnancy or other safety information.

Do you agree to waive the confidentiality given to you under the Market Research Codes of Conduct specifically in relation to any adverse event you report to us?

- ☐ Yes
- ☐ No

Waive confidentiality statement

If you agree to waive confidentiality, your name and contact details will be forwarded to the sponsor's pharmacovigilance department for the sole purpose of follow-up of such report(s). All other information that you give us in the context of this market research will continue to remain confidential. Are you willing to participate with the interview on this basis?

- ☐ I agree
- ☐ I do not agree

[PN: IF SELECT I AGREE AT WAIVE CONFIDENTIALITY STATEMENT] Thank you. Please note that if you provide your name during the adverse event reporting, this will not be linked in any way to your responses given during the interview.

We are obligated to share the manner in which your personal information will be handled and stored.
Any safety information we receive will be forwarded to the sponsor of this research for their records.
The sponsor will record any safety information including personal data received in their global database in the interests of patient safety and in compliance with all applicable global laws and regulations; and
During the reporting of safety information, the sponsor will not disclose such personal data to any un-associated third parties with the exception of any disclosures required by applicable law, regulation or the order of a competent authority

Please can you confirm if you agree to your personal details being stored for this purpose?

- ☐ I agree
- ☐ I do not agree

[PN: IF SELECT I DO NOT AGREE AT WAVE CONFIDENTIALITY STATEMENT] If we become aware of a reportable adverse event we are obliged to report this to the pharmaceutical company. We will file this report without giving any of your details, but if the Drug Safety Department requires more information, may we contact you again (without identifying you to the pharmaceutical company)?

- ☐ Yes

☐ No

Introduction

Thank you for taking the time to reflect and comment on your experiences of treating patients with fixed combination of basal insulin/GLP-1 (IDegLira).

All answers that you provide will be treated in the strictest confidence and your identity will not be revealed to any third parties. The results from your interview will be aggregated with those provided by other respondents. The aggregated results may be used in publications by the survey sponsor.

Your answers will be treated as anonymous and confidential.

Please respond to the questions by ticking the answer that best reflects your experience. There are no right or wrong answers to any of these questions.

Screener & Caseload Information

1. What is your profession *(Check one)*

Primary Care	i1. General Practice
	i2. Family Practice
	i3. Internal Medicine
	i4. Nurse
	i5. Other – Primary care
Secondary care	i6. General practice and certified as endocrinologist
	i7. General practice and certified as diabetologist
	i8. Family Practice and certified as endocrinologist
	i9. Family Practice and certified as diabetologist
	i10. Internal Medicine and certified as endocrinologist
	i11. Internal Medicine and certified as diabetologist
	i12. Endocrinologist
	i13. Diabetologist
	i14. Specialist Nurse
	i15. Other – Secondary care

*Should you choose 'Other' as one of your answers, you will have a chance to specify that answer on the next screen.

Single response only
If Q1_i5 or Q1_i15 selected then ask "Please specify your medical specialty"

Open text

2. How many **type II diabetes patients** do you treat on average **per month**?

   i1. Less than 50
   i2. 50-99
   i3. 100-149
   i4. 150-199
   i5. More than 200

Single response only

3. Approximately, what is the split of patients, treated by you, who are assigned to each of the following treatment regimens after basal insulin?

	% of type II diabetes patients
i1. Basal + bolus (+/- OAD)	
i2. Basal + GLP-1 (+/- OAD)	
i3. IDegLira (+/- OAD)	
i4. Premix (+/- OAD)	
i5. Other	
Total (max 100%):	100%

*Should you fill in 'Other' as one of your answers, you will have a chance to specify that answer on the next screen.

Numeric response (3 digits)
If total ≠ 100 then alert: "Please total up to 100%"
If Q4_i5 > 0 then ask: "Please specify the other treatment regimen"
Open text
If Q4_i3 = 0 then THANK&CLOSE
If sum of (Q4_i1 + Q4_i2 = 0) then THANK&CLOSE
If Q4_i3 = 0 AND sum (Q4_i1 + Q4_i2 = 0) then THANK&CLOSE

4. About how many patients have you treated with **IDegLira** in your clinic?

   i1. 0-1
   i2. 2-5
   i3. 6-10
   i4. 11-15
   i5. 15+

Single response only
If Q5_i1 selected thank THANK&CLOSE

Average patient information

Please answer the below questions thinking about an **"average" Type-2 Diabetes patient** who has no major comorbidities, aged 35-70 years, with average cognitive ability/normal mental status, and BMI equal to 25 or higher.

5. What treatment(s) was the patient receiving prior to treatment with **IDegLira**? *(Please tick all that apply)*

    i1. OADs
    i2. GLP-1
    i3. Basal (+/- OAD)
    i4. Basal + bolus (+/- OAD)
    i5. Basal + GLP-1 (+/- OAD)
    i6. Premix (+/- OAD)
    i7. Other

    *Should you choose 'Other' as one of your answers, you will have a chance to specify that answer on the next screen.

    Multiple responses possible
    If Q6_i7 selected then ask "Please specify the other treatment"

6. What would have been the most relevant alternative if you had not prescribed **IDegLira**? *(Please tick all that apply)*

    i1. Stay on OADs
    i2. Up-titrate GLP-1 (+/- OAD)
    i3. Up-titrate on basal (+/- OAD)
    i4. Basal + bolus (+/- OAD)
    i5. Basal + GLP-1 (+/- OAD)
    i6. Premix (+/- OAD)
    i7. Basal+ SGLT-2
    i8. Other

    *Should you choose 'Other' as one of your answers, you will have a chance to specify that answer on the next screen.

    Multiple responses possible
    If Q7_i8 selected then ask "Please specify the other treatment choice"
    Open text

7. Approximately, what is the split between your **main reasons** to prescribe **IDegLira** to your patients?

	Split in %
i1. Patient had uncontrolled blood glucose (HbA1c)	
i2. Patient had problems with hypoglycaemia	
i3. Patient had problems with gaining weight	

i4. Patient found previous treatment too complex	
i5. Patient expressed prior problems with nausea or other GI side effects	
i6. Other	
Total (max 100%):	

*Should you fill in 'Other' as one of your answers, you will have a chance to specify that answer on the next screen.

Numeric response (3 digits)
If total is ≠ 100% then alert "Please total up to 100%"
If Q8_i6 > 0 then ask "Please specify the other reason to prescribe IDegLira"
Open text

9. At the time of first prescribing **IDegLira**, what was the patient's HbA1c level?

   HbA1c level: ___%

   Numeric response (3 digits)
   If Q9 < 6% or Q9 > 15% then alert: "The HbA1c level has to be within the range 6 – 15%"

10. At the time of first prescribing **IDegLira**, what was the patient's weight?

    Weight:___kg

    Numeric response (3 digits)
    If answer < 45 or > 300 then alert "The answer has to be within the range 45-300kg"

11. Was the patient prescribed **IDegLira** at the same visit when introduced to **IDegLira** treatment option?

    i1. Yes
    i2. No

    Single response only
    If Q11_i1 selected then go to Q12
    Show Q11a and Q11b on the same screen

11a. Please specify the total number of visits it took for the patient to agree to initiate **IDegLira** treatment:

Visits:___

Numeric response (3 digits)

11b. How long did it take to initiate treatment with **IDegLira**?

__months and__weeks

Numeric responses, (2 digits)

12. Did the patient reach their target HbA1c level with **IDegLira**?

    i1. Yes
    i2. No

Single response only

13. What was the target HbA1c level?

HbA1c level: ___%

Numeric response 3 digits
If Q13 < 6% or Q13 > 15% then alert: "The HbA1c level has to be within the range 6 – 15%"
If Q12 = i2 then go to Q16A

14. How many visits did it take for the patient to reach their target level of HbA1c?

    i1. Number of visits___
    i2. Number of phone calls___

Show Q14 and Q14a on same screen
Numeric responses, 2 digits

14a. How long did it take for the patient to reach their target level of HbA1c?

__months and__weeks

Numeric responses, 2 digits

15. Please indicate what was the daily **IDegLira** dose, when the patient was in glycemic control? Please enter the value from 1 to 50 dose steps."

Number of dose steps:___
Numeric responses, 2 digits

If Q15 < 1 or > 50 then alert: "The number of dose steps has to be within the range 1 - 50"

15a. You mentioned: [Set the value from Q15] dose steps in the previous question, which means [Set the value from Q15] units of Insulin Degludec and Set the value form Q15*0.036] mg of liraglutide. Is that correct?

    i1. Yes

i2. No

If Q15_i2 selected then go to Q15

16. How many blood glucose measurements did you instruct your patient to take when using **IDegLira**? *Check one per column)*

	(1) Before reaching target HbA1c level	(2) After reaching target HbA1c level
i1. Once a week		
i2. Twice a week		
i3. Once a day		
i4. Two times a day		
i5. Three times a day		
i6. Four times a day		

Single choice per column

16A How many blood glucose measurements did you instruct your patient to take when using **IDegLira**? *(Check one)*

i1. Once a week
i2. Twice a week
i3. Once a day
i4. Two times a day
i5. Three times a day
i6. Four times a day

Single response only

17. Approximately, what is the split between the **main reasons** for your patients not reaching the target level of HbA1c with **IDegLira**? *(Please total up to 100%)*

	Split in %
i1. Patient has just initiated the treatment	
i2. Lack of adherence	
i3. Patient experienced nausea or other GI side effects	
i4. Fear of hypoglycemia	
i5. Fear of weight gain	
i6. Difficulties with titration	
i7. Difficulties with the device	
i8. Other	
Total (max 100%):	

*Should you fill in 'Other' as one of your answers, you will have a chance to specify that answer on the next screen.

Numeric response (3 digits)
If total ≠ 100 % then alert "Please total up to 100%"
If Q17_i8 > 0 then ask "Please specify the other reason for your patient not reaching the target level of HbA1c"
Open text

18. Did the patient discontinue the treatment with **IDegLira**?

    i1. Yes
    i2. No

19. Please indicate what percentage of your type-2 diabetes patients discontinues treatment with **IDegLira**?

    Percent of patients ___ %

    Numeric response, 3 digits
    If Q19 > 100% then alert: "The percentage has to be within the range 0 - 100"
    If Q19 = 0 % then go to Q22

20. How long after the initiation of the treatment did the patient discontinue?

    i1. After 0-3 months
    i2. After 4-6 months
    i3. After 7+ months

    Single response only

21. Approximately, what is the split between the **main reasons** for discontinuation of **IDegLira**?

	Split in %
i1. Lack of effect on blood glucose control (HbA1c)	
i2. Increased rate of hypoglycaemia	
i3. Level of patient co-pay	
i4. Lack of treatment adherence	
i5. Patients reached maximum dose steps of 50 units of IDegLira	
i6. Nausea or other GI side effects	
i7. Difficulties with titration	
i8. Difficulties with the device	
i9. Weight gain	

i10. Other	
Total (max 100%):	

*Should you fill in 'Other' as one of your answers, you will have a chance to specify that answer on the next screen.

Numeric response (3 digits)
If total ≠ then alert "Please total up to 100%"
If Q21_i10 > 0 then ask "Please specify the other reason for your patients not reaching the target level"
Open text

22. Thinking about concerns expressed by all of your patients treated with **IDegLira**, how often are the following mentioned by your patients:

	(1) Never	(2) Rarely	(3) Occasionally	(4) Regularly	(5) Always
i1. Fear of hypoglycemia					
i2. Fear of weight gain					
i3. Difficulty in calculating correct dose					
i4. Difficulty understanding dose steps					
i5. Feeling that the intensified regimen is too complicated					
i6. Difficulties with titration					
i7. Difficulties with the device					
i8. Difficulty remembering to take doses					
i9. Difficulty in taking dose at the right time					
i10. Difficulty adhering to intensified regimen					
i11. Difficulty carrying supplies throughout the day					

i12. Forgetting to take their insulin with them					
i13. Interference with daily life					
i14. Interference with their job performance					

Single response per row

Confidence level

The following questions ask about your **confidence with your patients' ability to titrate**.

23. How confident are you in up titrating a patient to reach their target level of HbA1c with **IDegLira**?

1 = Not at all confident	2 = Not very confident	3 = Neutral	4 = Confident	5 = Very confident

Single response
Scale 1 – 5

24. How confident are you in your patients 'ability to self-titrate their dosage on **IDegLira?**

1 = Not at all confident	2 = Not very confident	3 = Neutral	4 = Confident	5 = Very confident

Single response
Scale 1 – 5

25. Please compare your SATISFACTION of treating patients with IDegLira compared to Basal/Bolus based on each of the following:

	(1) Much more satisfied with **IDegLira**	(2) More satisfied with **IDegLira**	(3) Equally satisfied with both	(4) More satisfied with **Basal/ Bolus**	(5) Much more satisfied with **Basal/ Bolus**
i1. Reaching HbA1c target					
i2. Avoiding weight gain					
i3. Incidence of hypoglycaemia					
i4. Reaching fasting blood glucose target levels					
i5. Ease of training the patients					

i6. Time it takes to train patient on how to manage their injectable therapies					
i7. Overall side effect profile					
i8. Timing of dosing					
i9. Simplicity of therapy					
i10. Patient adherence					
i11. Number of injections					
i12. Patient satisfaction					

Single response per row

26. Based on your experience, how motivated are patients to reach their target blood glucose levels with **IDegLira** compared to **Basal/Bolus**?

(1)	(2)	(3)	(4)	(5)
IDegLira has much more potential to improve motivation	**IDegLira** has a little more potential to improve motivation	**IDegLira** is somewhat the same as **Basal/Bolus**	**Basal/Bolus** has a little more potential to improve motivation	**Basal/Bolus** has much more potential to improve motivation

Single response only

27. Based on your experience, what are your concerns for treating patients with **Basal/Bolus** compared with **IDegLira**?

	(1) Much more concerned with **IDegLira**	(2) More concerned with **IDegLira**	(3) Equally concerned with both	(4) More concerned with **Basal/ Bolus**	(5) Much more concerned with **Basal/ Bolus**
i1. Concern of patients having hypoglycemia					
i2. Concern of patients gaining weight					
i3. Concern of patient struggling with nausea and other GI side effects					

Single response per row

28. Based on your experience, how important is **full day Post Prandial Glucose (PPG) coverage** compared to **only main meal PPG coverage?**

(1)	(2)	(3)	(4)	(5)
Full day PPG coverage is much more important	**Full day PPG coverage** is more important	Somewhat the same important	**Main meal** PPG **coverage** is more important	**Main meal** PPG **coverage** is much more important

Single response per row

Thank you very much for completing the survey.