Pancreatic cancer and incretin therapy (GLP-1 and DPP-4)  June 2013

**Key points**

- There is a suggestion of a link in recent articles (1,2) between use of incretin therapy (GLP-1 and DPP-4), pancreatitis, and carcinoma of the pancreas;
- The methodology of the research has given rise to some discussion among specialists and there is consensus that the research findings, though interesting, have limitations;
- Currently there is no proven link between use of incretin therapy and pancreatic cancer;
- Following the most recent study (2) the FDA issued an early stage warning and both the FDA and the EMA are undergoing further independent research. Their advice is to continue taking the medications;
- Diabetes UK does not advocate any change in management on the basis of the publication and await more research on the subject. In particular, patients should NOT stop their medication on the basis of this report, unless advised to by their doctor. At the same time vigilance is required of patients on such therapies for any side effects suggestive of pancreatic disease.
- It is very important, as always, that any medication, particularly relatively modern therapies, such as incretin therapy, should be used in line with current guidance for appropriate patients. Subsequent monitoring of outcomes should also be acted upon in keeping with guidance, stopping treatment where therapy is not shown to have the agreed benefits.

**Introduction**

All drugs undergo careful testing under research trial conditions before they are licensed for use. However, these trials generally involve relatively small numbers of participants for short periods of time. Common side effects generally come to light during such testing, but rare side effects are usually not identified until the drug is used in routine clinical practice, in large numbers of people for long periods.

In diabetes, trials of drugs usually look at effects on “intermediate endpoints” which change quickly, such as glucose control or weight. Information about their effects on hard
outcomes such as heart disease or retinopathy takes much longer to gather and so is usually not available for some years after the drug is licensed.

Thus the decision to use any new drug in diabetes must involve weighing up the known and potential benefits against the known and unknown side-effects.

There is a suggestion of a link in recent articles (1,2) between use of incretin therapy, pancreatitis and carcinoma of the pancreas. This position statement aims to weigh up current evidence in order to make recommendations for clinicians as well as people with diabetes taking incretin therapy.

### Current situation

One study has suggested a potential risk of asymptomatic chronic pancreatitis and, with time, pancreatic cancer (1) with incretin therapy, compared to older agents. However, reporting bias cannot be excluded, as adverse events are more likely to be reported with newer agents. In addition, the methodology of the research has given rise to some discussion among specialists and there is consensus that the research findings, though interesting, have limitations.

Pancreatic cancer and pancreatitis are commoner in obese people (3) and in people with Type 2 diabetes (4). Acute and chronic pancreatitis, more common in people with Type 2 diabetes, are also risk factors for pancreatic cancer (5,6). Thus the study which found an increased risk of pancreatitis and pancreatic cancer with the two GLP-1 drugs available at the time (1) must be regarded with caution because of the complex relationships involved with obesity, diabetes, and treatments of diabetes. To put these risks into perspective, smoking is the commonest cause of pancreatic cancer and explains about 25% of the entire burden of disease with smokers having about a two-fold increased risk compared with non-smokers (7).

In conclusion, there is no proven link between use of incretin therapy and pancreatic cancer at present.

### Diabetes UK calls to action or Recommendations

Diabetes UK does not advocate any change in management of incretin therapy and await more research on the subject. In particular, patients should NOT stop their medication on the basis of this report, unless advised to by their doctor. At the same time vigilance is required of patients on such therapies for any side effects suggestive of pancreatic disease. These symptoms may include upper abdomen pain, jaundice, weight loss, nausea, loss of appetite and fever.

It also reminds clinicians and people with diabetes to be aware that incretin therapies are contraindicated in people with previous pancreatitis.
It is very important, as always, that any medication, particularly relatively modern therapies such as incretin therapy, should be used in line with current guidance for appropriate patients. Subsequent monitoring of outcomes should also be acted upon in keeping with guidance, stopping treatment where the therapy is not shown to have the agreed benefits. NICE guidance states that incretin therapy should only be continued if the person has had a beneficial metabolic response (8).

**Conclusion**

As there is no proven link between use of incretin therapies and pancreatic cancer Diabetes UK does not advocate any change in its management. In particular, patients should NOT stop their medication unless advised to by their doctor. At the same time vigilance is required of patients on such therapies for any side effects suggestive of pancreatic disease. It also reminds clinicians and people with diabetes to be aware that incretin therapies are contraindicated in people with previous pancreatitis.

**References**


6. Pancreatitis is a risk factor for pancreatic cancer Pradeep Bansal, Amnon Sonnenberg Gastroenterology 1 July 1995 (volume 109 issue 1 Pages 247-251)
