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The effect of time of day, fasting and meal type on biomarkers of liver injury in healthy subjects

Submission date 13/03/2021	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol [X] Statistical analysis plan [_] Results [_] Individual participant data [_] Record updated in last year
Registration date 06/04/2021	**Overall study status** Completed	
Last Edited 06/04/2021	**Condition category** Digestive System	

Plain English summary of protocol
Background and study aims
When new drugs are given to patients, it is important to monitor liver function and liver injury in case the new drug affect liver health. However, the food that patients eat can also influence liver function. Therefore, this study aimed to determine how diet alone can affect liver function.

Who can participate?
Healthy volunteers between the ages of 18-55 years could participate.

What does the study involve?
There were three phases of the study. In each phase, participants randomly received one of four possible diets for eight days (1) standard diet, (2) standard high-calorie diet, (3) high-fat high-calorie diet, and (4) high carbohydrate high-calorie diet. Participants then returned to their normal diets for 11 days before being randomized to a different diet for another 8 days. This process was done so that each participant received three different diets. Assessments included molecular markers of liver function, liver injury, and lipids over time.

What are the possible benefits and risks of participating?
Healthy volunteers who enrolled in this study were at minimal risk for adverse events.

Where is the study run from?
Pfizer Clinical Research Unit in New Haven, CT, USA.

When is the study starting and how long is it expected to run for?
February 2017 to September 2017

Who is funding the study?
Pfizer Inc (USA)

Who is the main contact?
Sanela Tarabar, sanela.tarabar@pfizer.com

Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
A9001500

Study information

Scientific Title
A randomized study to assess the effect of high-calorie, high-carbohydrate, and/or high-fat diet on biomarkers of liver injury in healthy volunteers

Study objectives
This study aimed to determine the effect of different food type regimens on biomarkers of hepatocellular and hepatobiliary injury, as well as biomarkers of liver function and lipid profiles

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 01/06/2017, IntegReview Ethical Review Board (3815 S Capital of Texas Hwy, Suite #320, Austin, TX, 78704, USA; +1-512-326-3001; clientservices@integreview.com), ref: A9001500

Study design

Open-label randomized single-centre three-period four-sequence balanced incomplete block design study

Primary study design
Interventional

Secondary study design
Randomised cross over trial

Study setting(s)
Other

Study type(s)
Other

Participant information sheet
No participant information sheet available

Health condition(s) or problem(s) studied
Effect of diet on markers of liver injury in healthy individuals

Interventions
Each healthy volunteer received three different diets in one of four possible sequences (randomized 1:1:1:1 using a computer generated randomization schedule) each for 8 days, which was expected to be a sufficient duration to detect liver enzyme changes. The four possible diets included
(1) standard diet (3000 kcal, 55% carbohydrates, 30% fat,15% protein)
(2) standard high-calorie diet (4500 kcal, 55% carbohydrates, 30% fat, 15% protein)
(3) high-fat high-calorie diet (4500 kcal, 25% carbohydrates, 60% fat, 15% protein)
(4) high-carbohydrate high-calorie diet (4500 kcal, 65% carbohydrates, 20% fat, 15% protein)

During each period, participants spent 10 days (11 nights) at the Clinical Research Unit. Meals were administered at intervals of approximately five hours, except on Day 9, when participants fasted until 1 pm. This was followed by a non-resident washout of at least 11 days, during which participants consumed their usual diet.

Intervention Type
Other

Primary outcome measure
1. Hepatocellular injury biomarkers: ALT, AST, and glutamate dehydrogenase (GLDH) measured using blood test at baseline and Day 2, Day 3, Day 5, Day 8, Day 9 and Day 10
2. Hepatobiliary injury biomarkers: ALP and gamma-glutamyl transferase (GGT) measured using blood test at baseline and Day 2, Day 3, Day 5, Day 8, Day 9 and Day 10
3. Hepatic function biomarkers:
3.1. Total bilirubin measured using blood test at baseline and Day 2, Day 3, Day 5, Day 8, Day 9 and Day10
3.2. Fasting total bile acids using blood test at baseline and Day 2 with hourly measurement from Hour 1 to Hour 16, Day 2, Day 3, Day 5, Day 8 with hourly measurement from Hour 1 to Hour 16, Day 9 with hourly measurements from Hour 1 to Hour 16, Day 10
4. Total bile acids during the post-meal period (8am-1pm, 1pm-6pm, 6pm-8am) measured using

blood test at Day 9 during the post-meal period (from Hour 1 to Hour 6, Hour 6 to Hour 10, hour 10 to hour 24
5. Concentration of novel biomarkers (GLDH, micro RNA) measured using blood test at baseline and D2, Day 3, Day 5, Day 8, Day 9 and Day 10.

Secondary outcome measures
1. Total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), and triglyceride measured using blood test at baseline and Day 2, Day 3, Day 5, Day 8, Day 9 and Day 10
2. Total bile acids and triglycerides at baseline and hourly from 8 am - 1 pm on Day 8 (fed) and Day 9 (fasted) measured using a blood test
3. Concentrations of bilirubin, ALT, AST, GGT, ALP, total cholesterol, LDL, HDL, triglycerides, and creatine kinase (CK) measured using blood test at baseline and diet on Day 9 and Day 9 with fasting

Overall study start date
08/02/2017

Completion date
06/09/2017

Eligibility

Key inclusion criteria
1. Aged 18-55 years old
2. No clinically relevant abnormalities identified by the medical screening
3. Body mass index (BMI) of 17.5-30.5 kg/m²
4. Total body weight >50 kg
5. Smoked ≤5 cigarettes daily
6. Free from the use of prescription or non-prescription drugs/dietary supplements for at least seven days or five half-lives prior to the first study period

Participant type(s)
Healthy volunteer

Age group
Adult

Lower age limit
18 Years

Upper age limit
55 Years

Sex
Both

Target number of participants
12

Total final enrolment
12

Key exclusion criteria
1. Women of childbearing potential
2. History of regular alcohol consumption (>7 drinks/week [female] or >14 drinks/week [male] within six months of screening
3. Treatment with an investigational drug within 30 days or fice half-lives of the first study period
4. Blood pressure ≥140 mm Hg (systolic) or ≥90 mm Hg (diastolic) following at least five minutes supine rest
5. Consumption of alcohol, caffeine, and the use of nicotine-containing products were not permitted 24-hours prior to, and during, the resident periods of the study

Date of first enrolment
16/06/2017

Date of final enrolment
30/06/2017

Locations

Countries of recruitment
United States of America

Study participating centre
Pfizer Clinical Research Unit
1 Howe Street
New Haven
United States of America
06511

Sponsor information

Organisation
Pfizer (United States)

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Sponsor type

Industry

Website
https://www.pfizer.com

ROR
https://ror.org/01xdqrp08

Funder(s)

Funder type
Industry

Funder Name
Pfizer

Alternative Name(s)
Pfizer Inc., Pfizer Consumer Healthcare, Davis, Charles Pfizer & Company, Warner-Lambert, King Pharmaceuticals, Wyeth Pharmaceuticals, Seagen

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal.

Intention to publish date
30/06/2021

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.
Upon request, and subject to certain criteria, conditions, and exceptions (see https://www.pfizer.com/science/clinical-trials/trial-data-and-results for more information), Pfizer will provide access to individual de-identified participant data from Pfizer-sponsored global interventional clinical studies conducted for medicines, vaccines, and medical devices (1) for indications that have been approved in the US and/or EU or (2) in programs that have been terminated (i.e. development

for all indications has been discontinued). Pfizer will also consider requests for the protocol, data dictionary and statistical analysis pan. Data may be requested from Pfizer trials 24 months after study completion. The de-identified participant data will be made available to researchers whose proposals meet the research criteria and other conditions, and for which an exception does no apply, via a secure portal. To gain access, data requestors must enter into a data access agreement with Pfizer.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Statistical Analysis Plan	version v1.0	22/08/2017	06/04/2021	No	No