Betalutin®
(^{177}Lu-HH1)

Arne Kolstad

Oslo University Hospital Norway

May 15, 2017

Disclosures of: Arne Kolstad

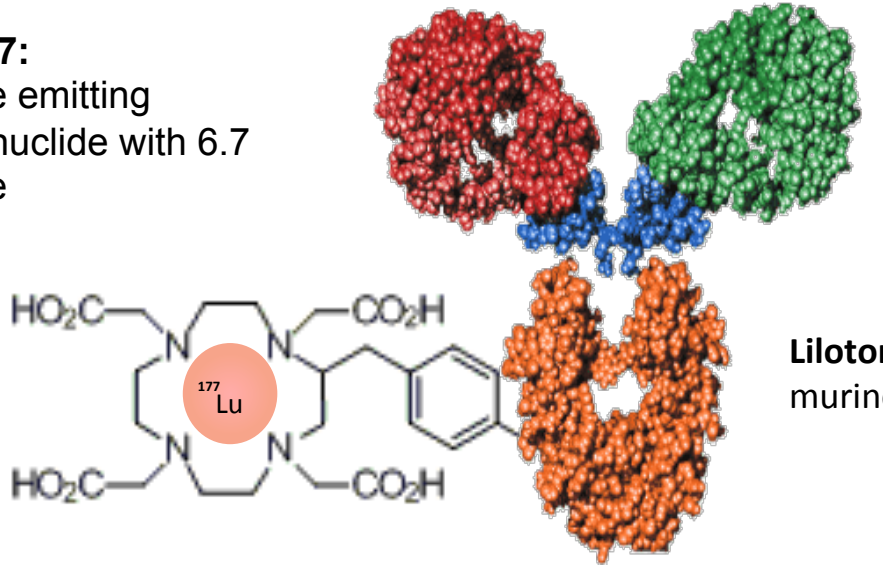
Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
Nordic Nanovector	Yes					Yes	

Background

- Patients with B cell NHL receive anti-CD20 antibody therapy as standard.
- RIT targeting CD20 (Zevalin® and Bexxar®) are not extensively used in treatment of NHL in spite of documented effects
- RIT targeting CD20 may not be as effective in patients who have been treated with anti-CD20 antibodies.
- Development of lilotomab (anti-CD37) and Lu177-lilotomab (Betalutin®) at Oslo University Hospital Radiumhospitalet

Betalutin®, a new anti-CD37 antibody radionuclide conjugate (ARC)

lutetium-177:
Beta-particle emitting radioactive nuclide with 6.7 days half-life



Lilotomab (HH1):
murine anti-CD37 antibody

satetraxetan:
Chelator that binds to lysine residues on lilotomab and chelates lutetium-177

4

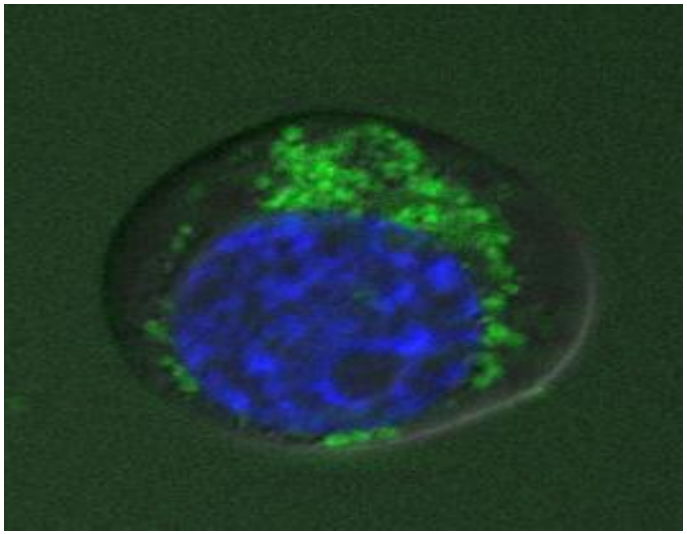
Change of radionuclide to lutetium-177

Feature	^{177}Lu	^{131}I (Bexxar)	^{90}Y (Zevalin)
Retained inside the cells after internalization?	Yes	No	Yes
Uptake of free radionuclide in body?	No	Thyriod	No
Can be imaged	Yes, low energy γ-photons	Yes, but high γ-energy	No
Need for shielding and isolation of patients?	No	Yes	No
Centralized production feasible?	Yes, half-life 6.7 days	Yes, half-life 8 days	No, too short half-life (2.7 d)
Long lived waste?	Not with n.c.a ^{177}Lu	No	No
Large amount of safety data before launch?	Yes*	No	No

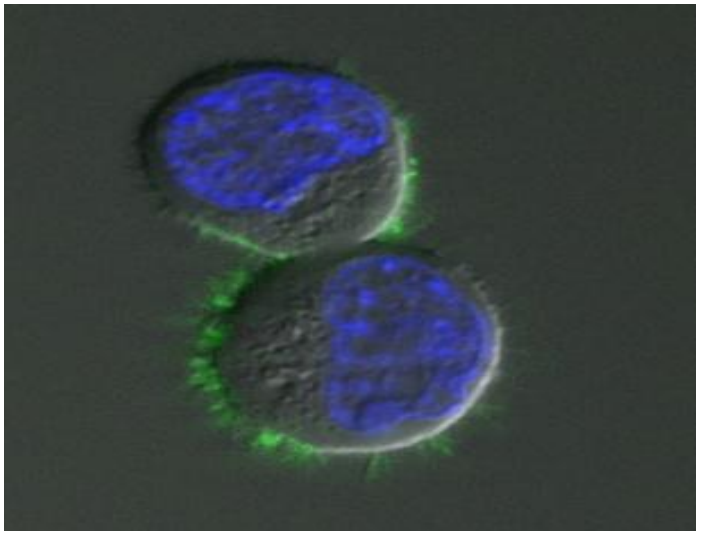
(*Mariniello et al., EJNMMI, 2016)

5

Anti-CD37 (tetulomab) is internalized while anti-CD20 (rituximab) is not internalized.



Ant-CD37



Anti-CD20

HH1 (Lilotomab): anti-CD37 antibody

- Antibody developed at the Norwegian Radium Hospital

Radiumhospitalet
Comprehensive Cancer Center

- Nordic Nanovector has obtained exclusive rights.

Clinical development of Betalutin

- More than 50 patients have been enrolled in to the LYMRIT-37-01 Phase 1/2 study
- Phase 1 study dose finding study in DLBCL patients is ongoing
- The latest trial data were presented at the ASH congress in December 2016

Kolstad A, et al. Presented at ASH, San Diego, December, 2016.

Centres from 9 countries across Europe are participating

Phase I & II – 9 centres

Norway
Oslo – Dr Kolstad
Trondheim - Dr. Fagerli
Bergen – Prof Bjørn
Croatia
Zagreb – Dr Aurer
Poland
Warsaw – Dr Walewski
Spain
Madrid - Dr Provencio Pulla
Salamanca - Dr Garcia-Sancho
Sweden
Umeå - Dr. Erlansson
UK
Manchester - Prof. Illidge

Phase II – 15 centres

Austria
Innsbruck - Dr. Willenbacher
Linz - Dr. Welterman
Vienna - Prof. Raderer
Czech Republic
Ostrava - Prof. Hajek
Olomouc - Prof. Papajik
Prague - Prof. Trnený
Italy
Firenze - Prof. Bosi
Bologna - Prof. Zinzani
Poland
Kraków - Prof. Jurczak
Warsaw - Prof. Jedrzejczak
Sweden
Linkøping - Dr. Lagerløf
Borås - Dr. Andersson
UK
Poole - Dr. Bayne
Glasgow - Dr. O'Rourke
Bristol - Dr. Beasley

Inclusion criteria

1. Histologically confirmed (by WHO classification) relapsed/ refractory incurable non-Hodgkin B-cell lymphoma of following subtypes; follicular grade I-IIIA, marginal zone, small lymphocytic, lymphoplasmacytic and mantle cell

2. Age > 18 years

3. A pre-study WHO performance status of 0-1

4. Life expectancy should be ≥ 3 months

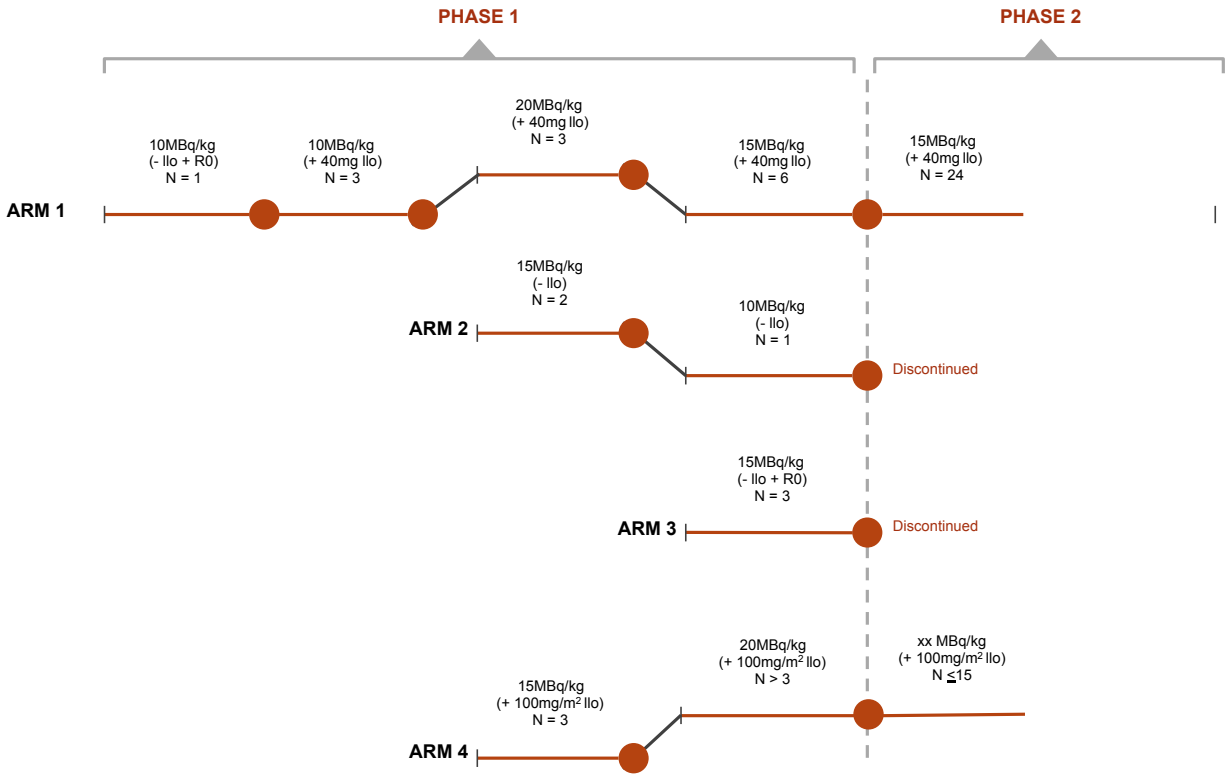
5. <25% tumour cells in bone marrow biopsy

6. Measurable disease by radiological methods

Exclusion criteria

1. Medical contraindications, including uncontrolled infection, severe cardiac, pulmonary, neurologic, psychiatric or metabolic disease, steroid requiring asthma/allergy, known HIV positive
2. Laboratory values within 15 days pre-registration:
   a. Absolute Neutrophil Counts $\leq 1.5 \times 10^9$ /l
   b. Platelet count $\leq 150 \times 10^9$ /l
   c. Total bilirubin ≥ 30 mmol/l
   d. ALP and ALAT $\geq$ 4x normal level
   e. Creatinine ≥ 110 µmol/l (men), 90 µmol/l (women)
3. Known CNS involvement of lymphoma

37-01 Study design



Summary of baseline characteristics

	10-20 MBq/kg N=38
Median Age years (range)	67 (41-80)
Male n (%)	24 (63%)
Female n (%)	14 (37%)
Histology	
Follicular Grade I	9
Follicular Grade II	15
Follicular Grade IIIA	4
Marginal Zone	8
Mantle Cell	3
Prior Therapies: median (range)	2 (1-8)

MBq = megabecquerel

Kolstad A, et al. Presented at ASH, San Diego, December, 2016

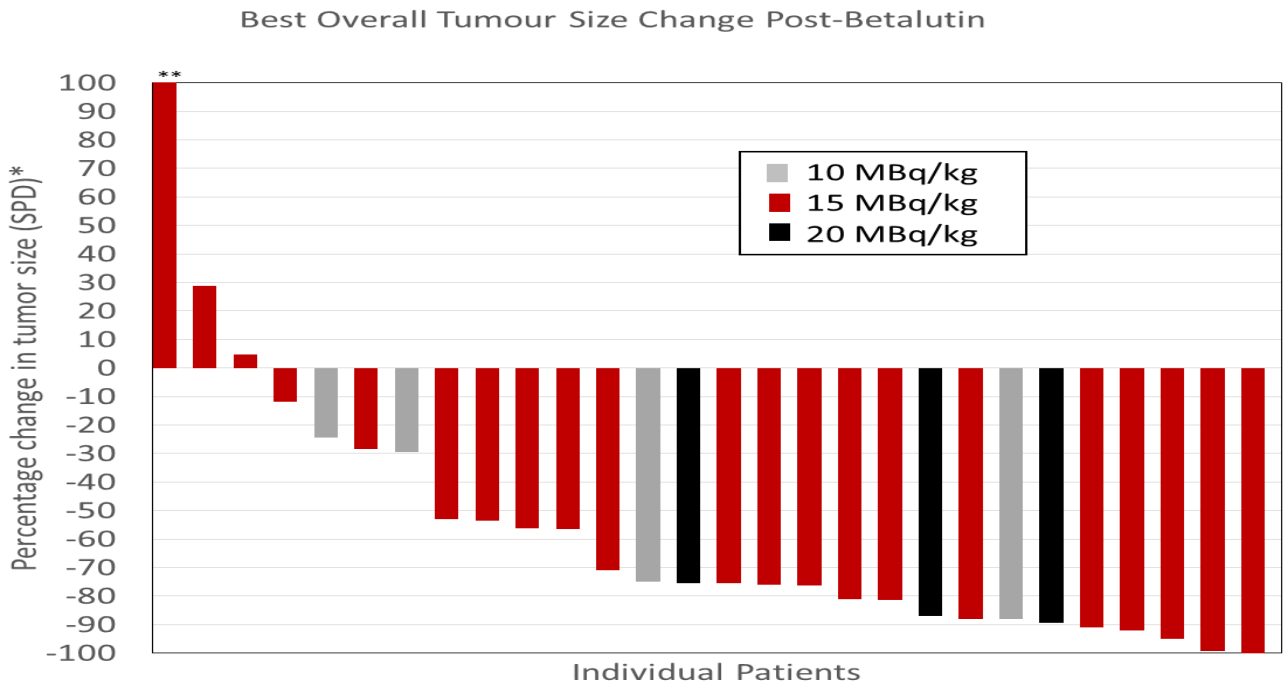
Total best response levels

	10-20 MBq/kg N=35 n (%)
Overall Response rate (CR + PR)	**22 (63%)**
Complete Remission (CR)	10 (29%)
Partial Remission (PR)	12 (34%)
Stable Disease (SD)	5 (14%)
Progressive Disease (PD)	8 (23%)

One patient had confirmed transformed lymphoma at 3 months.

Kolstad A, et al. Presented at ASH, San Diego, December, 2016.

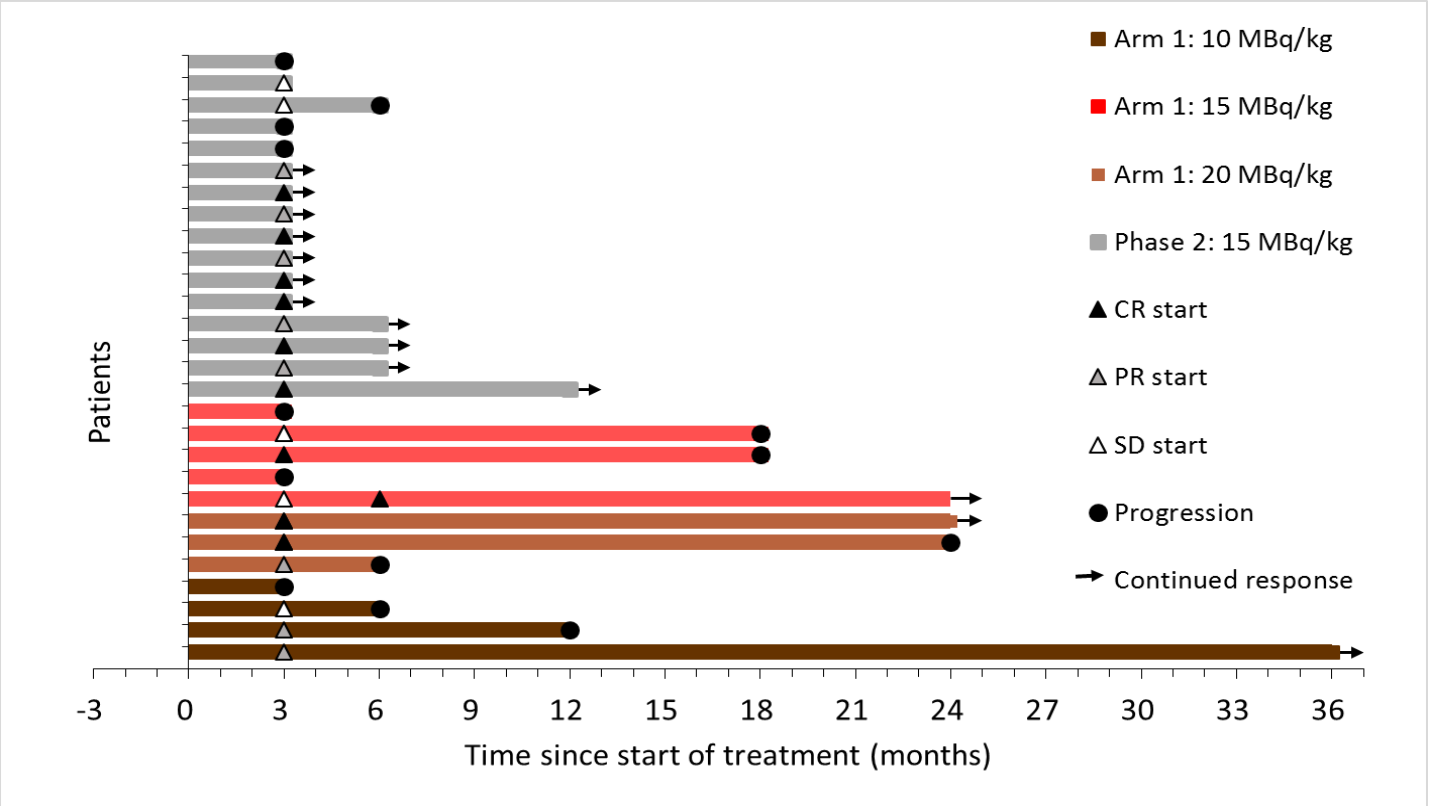
Maximum tumour size reduction



* SPD= Sum of the Products of the Diameters of the patients tumor
**=This patient had a tumor size increase of 180% truncated at 100% in this figure
One patient with a transofmred lesion has been ecluded from the analysis

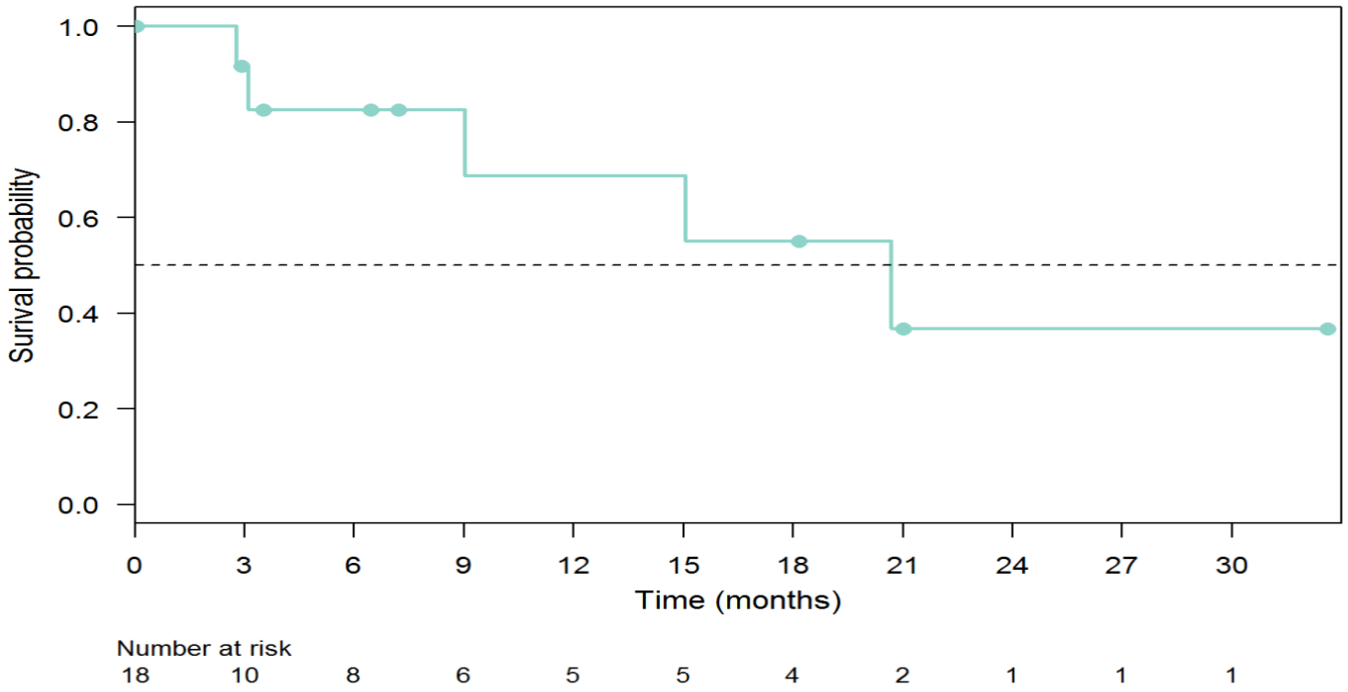
Kolstad A, et al. Presented at ASH, San Diego, December, 2016

Status of enrolled patients

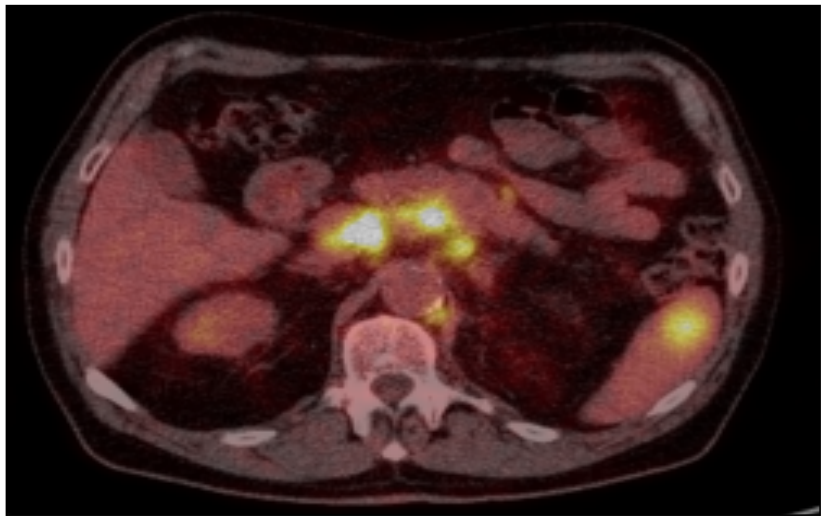


Kolstad A, et al. Presented at ASH, San Diego, December, 2016.

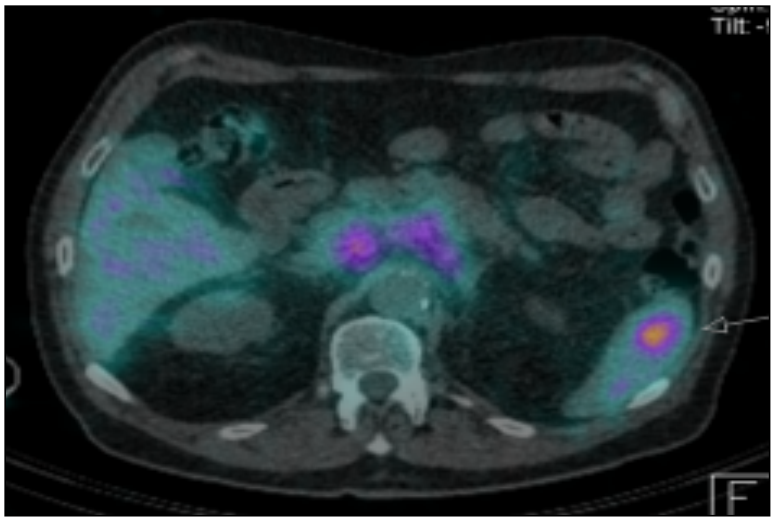
Median duration of response for Arm 1 patients (20.7 m)



Imaging results: FDG PET/CT and SPECT/CT scans



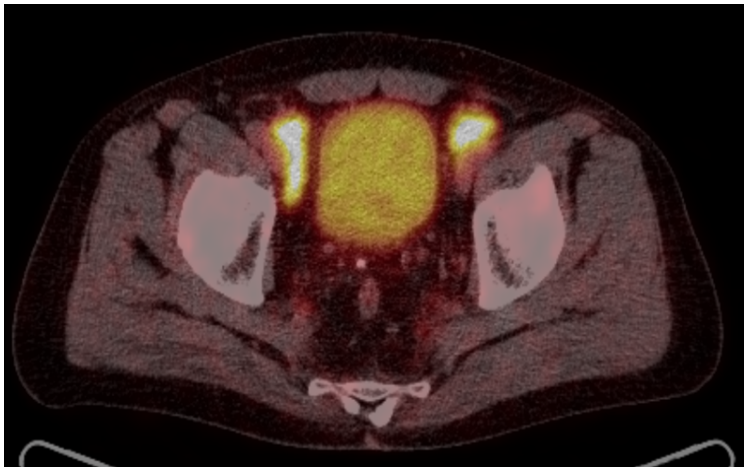
Baseline FDG PET/CT scan showing tumor locations



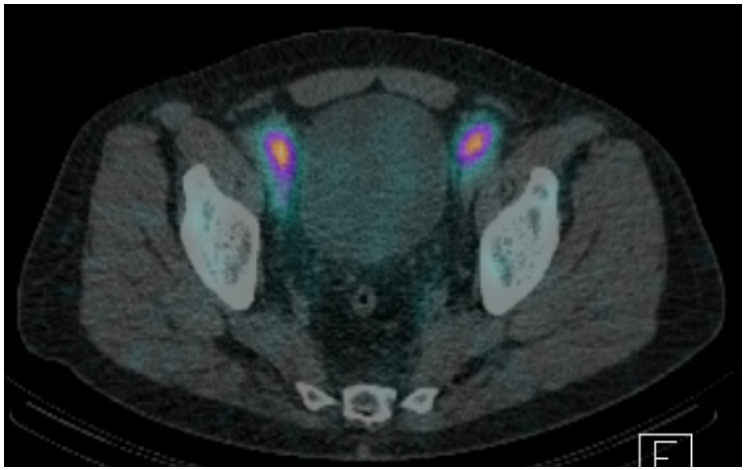
Day 5 SPECT/CT scan showing radioactivity uptake in tumors

FDG PET CT = fluorodeoxyglucose positron emission tomography-computer tomography; MBq = megabecquerel; SPECT = single-photon emission computerized tomography.

Imaging results: FDG PET/CT and SPECT/CT scans



Baseline FDG PET/CT scan showing tumor locations



Day 5 SPECT/CT scan showing Betalutin uptake in tumors

19

Summary

- Betalutin®, a single dose, ***ready-to-use formulation***, that binds to a novel target, CD37 for the treatment of NHL.
- Most Grade 3/4 AEs were haematological (thrombocytopenia and neutropenia), all transient and reversible.
- Promising efficacy and durable responses were observed.
- Betalutin® targets a different antigen than CD20 and has the potential to be a novel, safe and effective therapy for B-cell malignancies.