

## Abstract (Click on the text to edit)

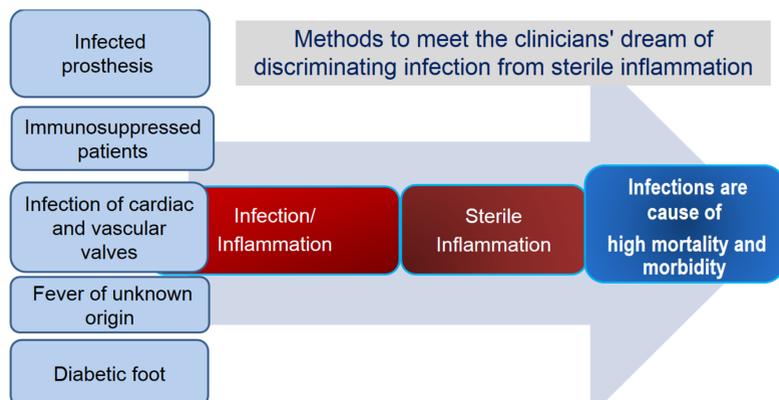
The cationic peptide UBI 29-41 derived from ubiquicidin, conjugated with NOTA and labeled with <sup>68</sup>Ga is able to discriminate infected (*S. aureus*) from sterile inflamed tissues in mice by PET/CT.

In order to evaluate its applicability in patients, a PET radiopharmaceutical was developed based on our previous preclinical investigations with <sup>68</sup>Ga-NOTA-UBI-29-41, and the previous results in patients with <sup>99m</sup>Tc-UBI-29-41.

<sup>68</sup>Ga-NOTA complex has a high thermodynamic and kinetic stability, which is associated with the fact that <sup>68</sup>Ga is a positron emitter available from a <sup>68</sup>Ge/<sup>68</sup>Ga generator, allowing to obtain <sup>68</sup>Ga-NOTA-UBI with high efficiency.

In adults and pediatric patients, the recommended amount of radioactivity to be administered for PET imaging is 2 MBq/kg of body weight (0.054 mCi/kg) up to 200 MBq (5.4 mCi) by intravenous injection.

## Background



## Objective

To optimize

- Formulation and semiautomatic production of <sup>68</sup>Ga-NOTA-UBI-29-41 under GMP conditions
- Methods for quality control

## Materials & Methods

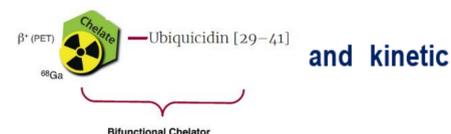
1000 MBq <sup>68</sup>GaCl<sub>3</sub> + 40 nmol UBI + sodium acetate buffer 0,25M pH 3,5-4,0, incubation 100 °C for 5 min. Purification Sep-Pak C18



## <sup>68</sup>Ga-NOTA-UBI-29-41: GMP Production

The PET radiopharmaceutical was developed based on:

- Our previous preclinical investigations <sup>68</sup>Ga-NOTA-UBI-29-41
- Previous results in patients with <sup>99m</sup>Tc-UBI-29-41
- <sup>68</sup>Ga-NOTA complex has **kinetic stability**



## Quality Control

Guidelines used for selecting quality control tests

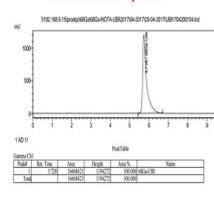
[European Pharmacopoeia \(Ph. Eur.\)](http://www.edqm.eu/en/Work-ProgrammeStatus-607.html)  
<http://www.edqm.eu/en/Work-ProgrammeStatus-607.html>

[United States Pharmacopoeia \(USP\)](http://www.usp.org/)  
<http://www.usp.org/>

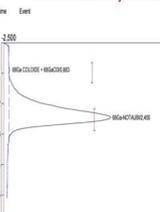
- ☑ Visual Inspection  
Transparent and colorless
- ☑ pH
- ☑ Radionuclidic Purity and Identity
- ☑ Radiochemical Purity and Identity  
> 90% HPLC/ITLC
- ☑ Pyrogen
- ☑ Sterility
- ☑ Toxicity
- ☑ Filter Integrity
- ☑ Chemical Purity -Residual solvents GC

<sup>68</sup> GaNOTA UBI 17042001	QC Specifications	Results
Visual	Colorless, transparent, no particles	C
pH	4.0-8.0	7.5
Radiochemical Purity Global-HPLC + TLC	> 90 %	99.9
Radiochemical Purity - HPLC	-----	100
HPLC Identity	Ir estándar = Ir muestra (min)	5.7
HPLC + TLC Impurity A ( <sup>68</sup> Ga(OH)3)	A ( <sup>68</sup> Ga(OH)3) + B ( <sup>68</sup> GaCl3) < 10%	0.1
HPLC Impurity B ( <sup>68</sup> GaCl3)	A ( <sup>68</sup> Ga(OH)3) + B ( <sup>68</sup> GaCl3) < 10%	ND
Chemical Purity GC	Ethanol < 10%	7.4
Radionuclidic purity (spectrum)	99.5 % at 511 keV and/or 1077 keV	C
Radionuclidic purity ( <sup>68</sup> Ge content)	< 0.001%	0,000043%
Radionuclidic Identity T <sub>1/2</sub> (min)	62-74	68
Pyrogen	<25 EU/mL (< 175 EU/Vol)	<10
Sterility	Culture	No growth

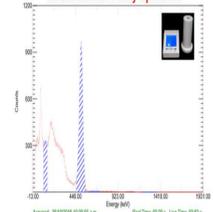
### Radiochemical Purity-HPLC



### Radiochemical Purity-TLC-SG



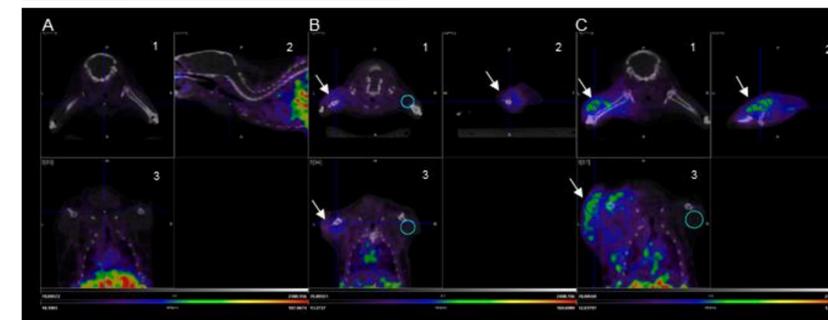
### Radionuclidic Purity-Spectrum



### Endotoxin detection system

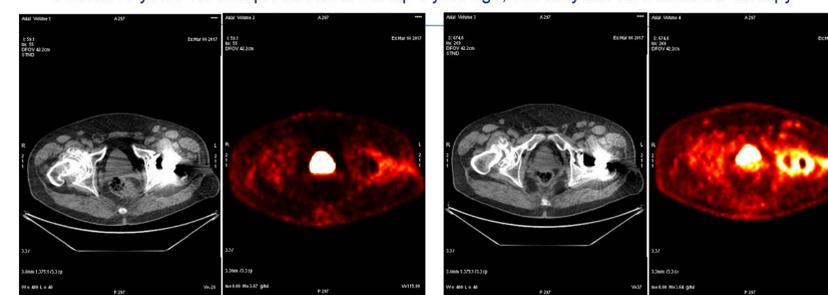


	T/NT		
	30 min	60 min	120 min
INFECTED	3,49	4,96	4,06
INFLAMMED	1,90	1,57	1,20
HEALTHY	1,03	1,23	1,06



## First patient with <sup>68</sup>Ga-UBI and <sup>18</sup>F-FDG

Patient 50 years old with prosthesis in left hip 1 year ago, currently infection with ATB therapy



<sup>68</sup>Ga-UBI <sup>18</sup>F-FDG  
Images by Javier Gaudio, Javier Vilar, Agustina Banchemo, Justino Menendez (CUDIM)

## Results

Radiochemical purity was higher than 95%. Yield of purification by solid phase extraction with Sep-pak C-18 was 63% and with Sep-pack C-18 plus was 75%. Specific activity was higher than 25MBq/nmol. Its appearance is colorless and particulate free. The formulation obtained is sterile and pyrogen free, and compatible with homeostasis in terms of pH and isotonicity. Final volume is 10 mL and activity concentration 49.8 MBq/mL.

A new radiopharmaceutical: <sup>68</sup>Ga-NOTA UBI-29-41, was developed and is suitable for use in clinical trials in patients for which approval has already been obtained from the CUDIM ethics committee.

## Conclusion

The novel tracer, suitable for use in clinical trials, was developed with the aim of discriminate bacterial infection from inflammation.

## References

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**<sup>68</sup>Ga-NOTA-UBI 29-41 as a PET tracer for detection of bacterial infection**

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