# Y90 Glass Microsphere Treatment for iCCA: Final Results from the Largest Prospective Real-World Study (PROACTIF)

Boris Guiu[1], Ghoufrane Tlili[2], Clément Bailly[3], Eric Vibert[4], Julia Chalaye[5], Denis Mariano-Goulart[1], Julien Edeline[6], Jean Frederic Blanc[2], Yann Touchefeu[3], Gilles Grimon[7], Hélène Regnault[5], Julie Roux[8], Antoine Bouvier[9], Isabelle Brenot-Rossi[10], Géraldine Sergent[11], Stephane Renaud[12], Sylvain Manfredi[13], Arnaud Dieudonné[14], **Kirk Fowers[15]**, Eric Vicaut[16], Etienne Garin[6], and the PROACTIF investigators group

[1]Hôpital Saint-Eloi, Montpellier, France; [2]Hôpital du Haut-Lévêque, Bordeaux, France; [3]Centre Hospitalier Universitaire de Nantes, Hôpital Hotel-Dieu, Nantes, France; [4]AP-HP, Hôpital Paul Brousse, Villejuif, France; [5]CHU Hôpital Henri-Mondor, Créteil, France; [6]Centre Eugène Marquis, Rennes, France; [7]Bicêtre Hôpital, Le Kremlin-Bicêtre, France; [8]Centre Hospitalier Universitaire de Grenoble Alpes, Grenoble, France; [9]Centre Hospitalier Universitaire de Angers, Angers, France; [10]Institut Paoli-Calmettes, Marseille, France; [11]Centre Hospitalier Universitaire de Lille, Hôpital Claude Huriez, Lille, France; [12]Centre Hospitalier de Perpignan, Hôpital Saint Jean, Perpignan, France; [13]Centre Hospitalier Universitaire de Dijon, Dijon, France; [14]Centre Henri Becquerel, Rouen, France;[15] Boston Scientific Corporation, Marlborough, MA, USA; [16]AP-HP Groupe Hospitalier Lariboisière – Fernand-Widal, Paris, France

## Background

**PROACTIF:** A **Pro**spective, Post-**A**pproval, Multi-centre, Open-Label, Non-Interventional Registry Study to Evaluate Effe**c**tiveness of **T**heraSphere™ in Cl**i**nical Practice in **F**rance

**Study Objective**: This study evaluated the effectiveness, safety, and dosimetry of selective internal radiation therapy with Y90 in a real-world clinical setting. Herein, we present the final data for iCCA.

**Enrollment**:
- Intrahepatic cholangiocarcinoma (**iCCA**; n=207) patients from 30 French institutions underwent Y90 treatment after consenting to data collection

## Methods

- Patients were treated with Y-90 per local procedures with protocol guidance on treatment method and tumor dose

**Primary Endpoint**:
- OS assessed by Kaplan-Meier analysis

**Key Secondary Endpoints**:
- Grade ≥ 3 adverse events (**AEs**) and serious AEs (**SAEs**)
  - Assessed using CTCAE v5
- Prior and concomitant treatment
- Subsequent treatment
- Dosimetry planning
  - Administered activity selected by investigator

## Results

**Table 1.** Patient Demographics and Tumor Characteristics

| Variable | N = 207 n(%) |
|---|---|
| **Age**[1], median (IQR) | 69.0 (62.0 – 76.0) |
| **Albumin-Bilirubin (ALBI) Grade**[1] | |
| 1 | 109 (52.7) |
| 2 / 3 | 47 (22.7) / 2 (1.0) |
| Missing | 49 (23.7) |
| **ECOG Score**[1] | |
| 0 / > 0 | 117 (56.5) / 75 (36.2) |
| Missing | 15 (7.2) |
| **Child Pugh Score**[1] | |
| A / B | 93 (44.9) / 7 (3.4) |
| **Total Number of Lesions**[2] | |
| 1 / > 1 | 109 (52.7) / 84 (40.6) |
| Missing | 14 (6.8) |
| **Index Lesion Diameter**[2,3] | |
| Median size, cm (IQR) | 7.0 (5-9.5) |
| ≤ 7 cm / > 7 cm | 91 (50.8) / 88 (49.2) |
| **Tumor Distribution**[1] | |
| Unilobar / Bilobar | 139 (67.1) / 55 (26.6) |
| Missing | 13 (6.3) |
| **Portal Vein Thrombosis**[2] **(PVT)** | 34 (16.4) |
| **Liver Disease**[1] | |
| Normal liver/no history | 115 (55.6) |
| Cirrhosis / fibrosis | 45 (21.7) / 21 (10.1) |
| Missing | 26 (12.6) |
| **Etiology of Underlying Liver Disease**[1,4] (Top 4) | |
| Alcohol | 39 (18.8) |
| Hepatitis B / C | 4 (1.9) / 6 (2.9) |
| No underlying disease | 135 (65.2) |
| Metabolic / MASH | 17 (8.2) / 9 (4.3) |

Abbreviations: **ECOG**, Eastern Cooperative Oncology Group; **IQR**, interquartile range; **MASH**, metabolic dysfunction-associated steatohepatitis
[1] Investigator assessment; [2]Central Assessment; [3]According to RECIST 1.1; [4]patients may have had more than one

**Table 2.** Treatment and Dosimetry

| Variable | N = 207 n(%) |
|---|---|
| **Prior Treatment**[1,2] | 77 |
| Systemic | 70 (90.9) |
| Locoregional | 7 (9.1) |
| Surgery | 10 (13.0) |
| **Concomitant Treatment** | |
| Yes | 70 (33.8) |
| **Dosimetry**[2] | |
| Single compartment | 66 (31.9) |
| Multicompartment | 141 (68.1) |
| **Pretreatment Dosimetry**[3] | |
| Mean Absorbed Dose (SD)to IL (Gy) | 357.0 (277.1) |

Abbreviations: IL, index lesion; SD, standard deviation
[1]Patients may have had more than one; [2]Investigator assessment; [3]Central assessment

**Table 3.** Overall Survival by Subgroups of Interest

| Subgroup | n | Median (95% CI[1]) |
|---|---|---|
| **TheraSphere Treatment** | | |
| First-line | 157 | **23.3 M** (21.0 – 29.2) |
| Second-line | 25 | **11.4 M** (7.1 – 17.2) |
| **Liver Status** | | |
| Cirrhosis/Fibrosis | 66 | **19.8 M** (14.9 – 27.6) |
| No Cirrhosis/fibrosis | 115 | **23.3 M** (18.1 – 26.3) |
| Unknown | 26 | **22.2 M** (16.7 – NE) |
| **Index Lesion Size, RECIST 1.1** | | |
| ≤ 7 cm | 91 | **22.6 M** (18.2 – 30.1) |
| > 7 cm | 88 | **23.7 M** (17.6 – 26.3) |
| **Number of Tumors** | | |
| 1 | 109 | **24.2 M** (22.2 – 37.9) |
| >1 | 84 | **17.2 M** (12.5 – 21.3) |
| **Concomitant Treatment** | | |
| Yes | 70 | **21.9 M** (16.8 – 37.1) |
| No | 115 | **21.3 M** (17.6 – 24.2) |

Abbreviations: **M**, months; **N**, number of patients; **NE**, not evaluable
[1]Brookmeyer and Crowley methodology

**Figure 1.** Overall Survival among all iCCA patients (A); and by subsequent treatment (B).

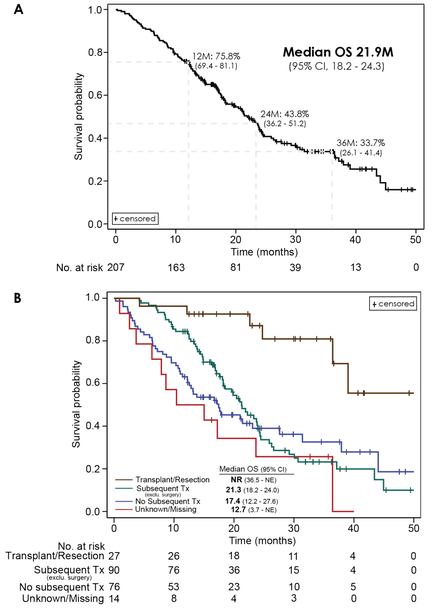


**Table 4.** AE Summary

| AE Type | n (%) | Total Events |
|---|---|---|
| Patients with ≥ 1 AE[1] | 15 (**7.2**) | 20 |
| Patients with ≥ 1 SAE[2] | 14 (**6.8**) | 18 |
| Patients with ≥ 1 related SAE | 8 (**3.9**) | 10 |

Abbreviations: AE, adverse event; n, number of patients; SAE, serious adverse event
[1] AEs were collected if they occurred within 90 days of Y90
[2] SAEs, related or not, were collected during the "initial 12-month period", then only related SAEs were collected during the "Follow-up Period"

### *Take home messages*

- Results show **meaningful survival benefit** and an **acceptable adverse event profile** for patients with and without cirrhosis
- Importantly, **TheraSphere Y-90 as a neoadjuvant to surgery** resulted in survival outcomes rarely observed in **initially unresectable patients**
- This real-world study demonstrates and confirms that Y-90 treatment plays a key role in the multimodal treatment strategies for iCCA

## BACKGROUND

PROACTIF confirms the safety and efficacy of TheraSphere to treat primary liver cancer in a real-world setting.

## METHODS

Patients agreed to share their health and treatment information with designated authorities for up to five years.

## RESULTS

Patients were treated using a tailored approach (including some receiving more than one treatment). Patients with intrahepatic cholangiocarcinoma treated with TheraSphere lived up to 49.5 months with limited side effects from treatment.

## CONCLUSION

TheraSphere treatment was safe and effective in patients with intrahepatic cholangiocarcinoma in a real world setting.