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# Phase I study of C-CAR031 (AZD7003), a GPC3-targeted TGFβRIIDN armoured autologous CAR-T, in advanced hepatocellular carcinoma: Updated results

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# Declaration of Interests

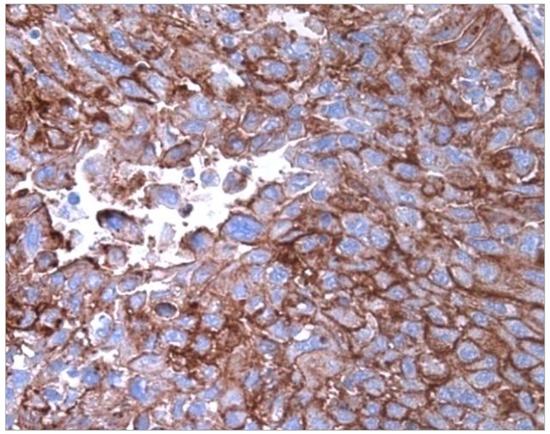
Y.Y and J.Huang are employees of AbelZeta Pharma, Gaithersburg, MD, USA. A.Z., Y.H. and Q.J. are employees of Shanghai AbelZeta, Shanghai, China. J.A., J.Hauser, X.Q. and S.D.V are employees of AstraZeneca. The other authors declare no competing interests.

# C-CAR031 (AZD7003): a dnTGFβRII armoured GPC3 CAR-T

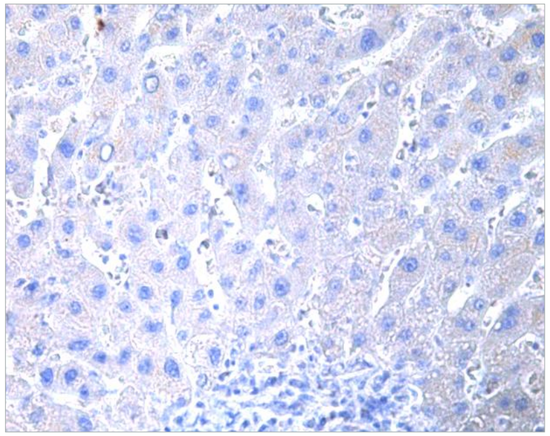
## GPC3 is an ideal HCC target

- Glypican-3 (GPC3) is highly expressed in the majority of HCC tumours and virtually absent in normal adult tissues[1,2,3]

**HCC tumour**

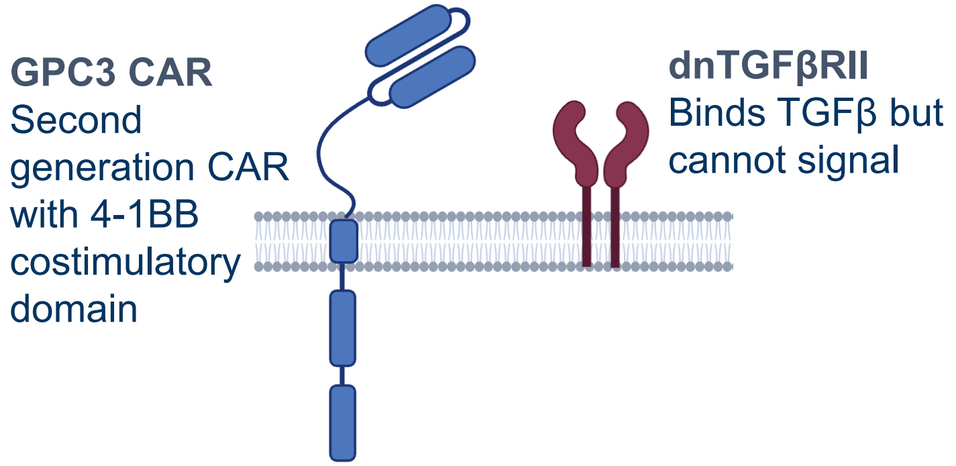


**Adjacent normal liver**



## C-CAR031 (AZD7003) design

- C-CAR031 is now known as AZD7003
- Affinity-tuned anti-GPC3 scFv enhances safety[4]
- Co-expression of a dominant negative (dn) receptor protects from TGFβ-driven immunosuppression[5,6]




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1. Moek KL et al, Am J Pathol. 2018 Sep;188(9):1973-1981; 2. Batra et al, Cancer Immunol Res. 2020 Mar;8(3):309-320; 3. Bergamaschi et al, AACR 2025, Abstract 3793; 4. Giardino Torchia ML et al, Cytotherapy. 2022 Jul;24(7):720-732; 5.Tauriello DVF et al, Nat Rev Cancer. 2022 Jan;22(1):25-44; 6. Zhang Q et al, Nature. 657, 495–504 (2026)

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# First-in-human study design

## Key Eligibility Criteria

- 18-75 years of age
- Histologically confirmed GPC3+ HCC
- BCLC B/C, Child-Pugh A
- Relapsed/progressed/intolerant to HCC systemic therapies (≥1 line)
- No active CNS involvement

## Key Endpoints

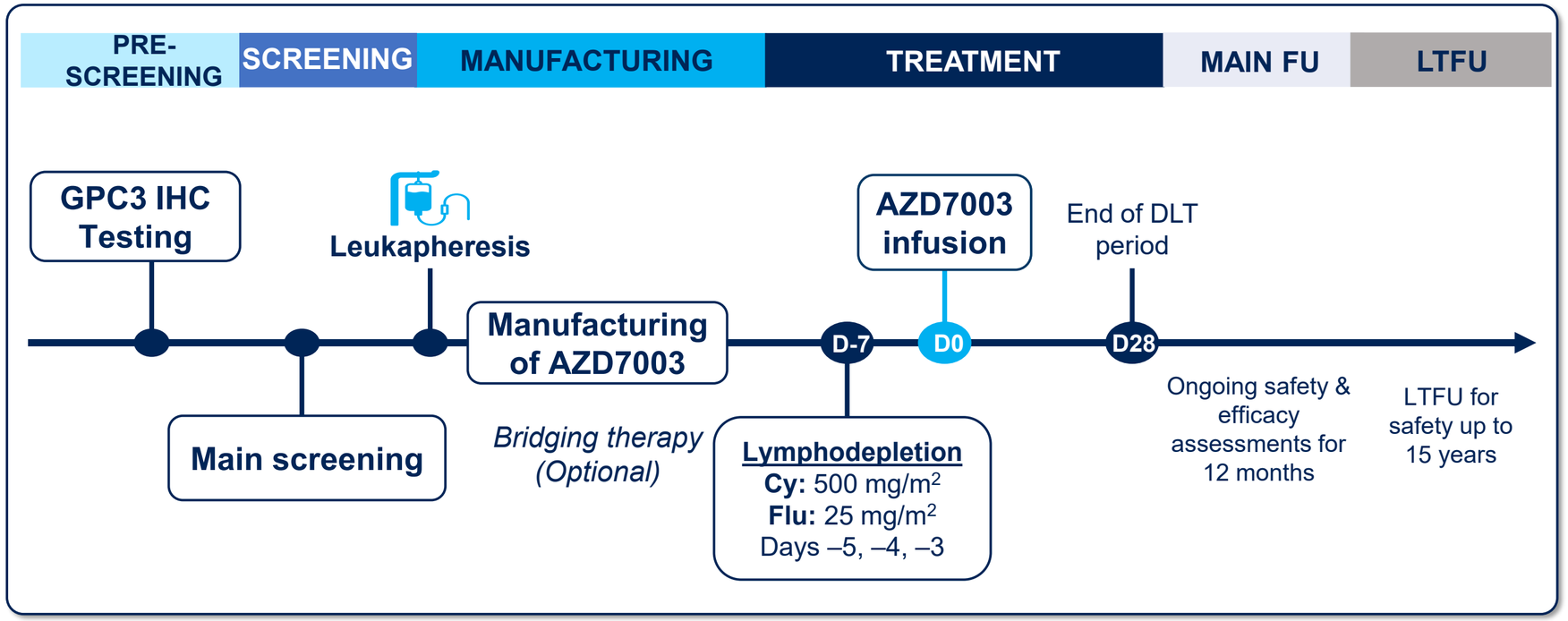
**Primary**

- Safety and tolerability (incidence and severity of TEAEs including DLTs)

**Secondary**

- Investigator-assessed ORR, DCR per RECIST v1.1, and OS

## Patient Journey




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BCLC, Barcelona Clinic Liver Cancer; CNS, central nervous system; Cy, cyclophosphamide; DCR, disease control rate; DLT, dose-limiting toxicity; Flu, fludarabine; FU, follow-up; IHC, immunohistochemistry; LTFU, long-term follow up; ORR, objective response rate; OS, overall survival; TEAE, treatment-emergent adverse event

# Demographic and baseline characteristics

## Heavily pre-treated advanced HCC patients, predominantly of HBV aetiology

| Characteristics | 0.75 × $10^6$ cells/kg N=1 | 1.5 × $10^6$ cells/kg N=6 | 2.5 × $10^6$ cells/kg N=18 | 4.0 × $10^6$ cells/kg N=11 | Overall N=36 |
|---|---|---|---|---|---|
| **Male, n (%)** | 1 (100) | 6 (100) | 15 (83.3) | 9 (81.8) | 31 (86.1) |
| **Median age, years (range)** | 50 | 48 (27, 62) | 51 (35, 70) | 53 (25, 59) | 51 (25, 70) |
| **ECOG PS, 0/1, n (%)** | 0 / 1 (100) | 0 / 6 (100) | 7 (38.9) / 11 (61.1) | 0 / 11 (100) | 7 (19.4) / 29 (80.6) |
| **BCLC Stage C, n (%)** | 1 (100) | 6 (100) | 16 (88.9) | 11 (100) | 34 (94.4) |
| **Child-Pugh Score, n (%)** | | | | | |
| • A (5-6) | 0 | 6 (100) | 18 (100) | 10 (90.9) | 34 (94.4) |
| • B (7-9)[a] | 1 (100) | 0 | 0 | 1 (9.1) | 2 (5.6) |
| **Cirrhosis, n (%)** | 1 (100) | 5 (83.3) | 12 (66.7) | 7 (63.6) | **25 (69.4)** |
| **HBV Infection, n (%)** | 1 (100) | 6 (100) | 17 (94.4) | 11 (100) | **35 (97.2)** |
| **AFP ≥400 ng/ml, n (%)** | 0 | 2 (33.3) | 12 (66.7) | 11 (100.0) | 25 (69.4) |
| **Intrahepatic lesions, n (%)** | 1 (100) | 4 (66.7) | 13 (72.2) | 8 (72.7) | 26 (72.2) |
| **Extrahepatic spread, n (%)** | **1 (100)** | **6 (100)** | **13 (72.2)** | **10 (90.9)** | **30 (83.3)** |
| **Median target lesion SLD (mm)[b], (range)** | **77.9** | **87.6 (13.3, 121.7)** | **52.9 (12.9, 125.3)** | **81.6 (33.6, 189.6)** | **69.9 (12.9, 189.6)** |
| **Median Number of Prior Lines of Therapies, (range)** | **4** | **2.5 (1, 6)** | **3 (1, 7)** | **5 (2, 8)** | **4 (1,8)** |
| • ≥3, n (%) | **1 (100)** | **3 (50.0)** | **11 (61.1)** | **10 (90.9)** | **25 (69.4)** |
| **Received both IO and VEGF(R) inhibitors[c]** | **1 (100)** | **5 (83.3)** | **16 (88.9)** | **11 (100)** | **33 (91.7)** |
| **Received bridging therapy, n (%)** | 0 | 3 (50.0) | 10 (55.6) | 7 (63.6) | 20 (55.6) |

Data cutoff 15 August 2026

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a. Data collected at baseline. All enrolled patients had Child-Pugh score A at screening, 2 patients subsequently reported Child-Pugh score B at baseline. b. Per RECIST1.1; c. IO defined as immune checkpoint inhibitors, and VEGF(R) inhibitors defined as anti-angiogenesis agents such as bevacizumab (or its biosimilars), TKIs such as sorafenib, lenvatinib and apatinib.

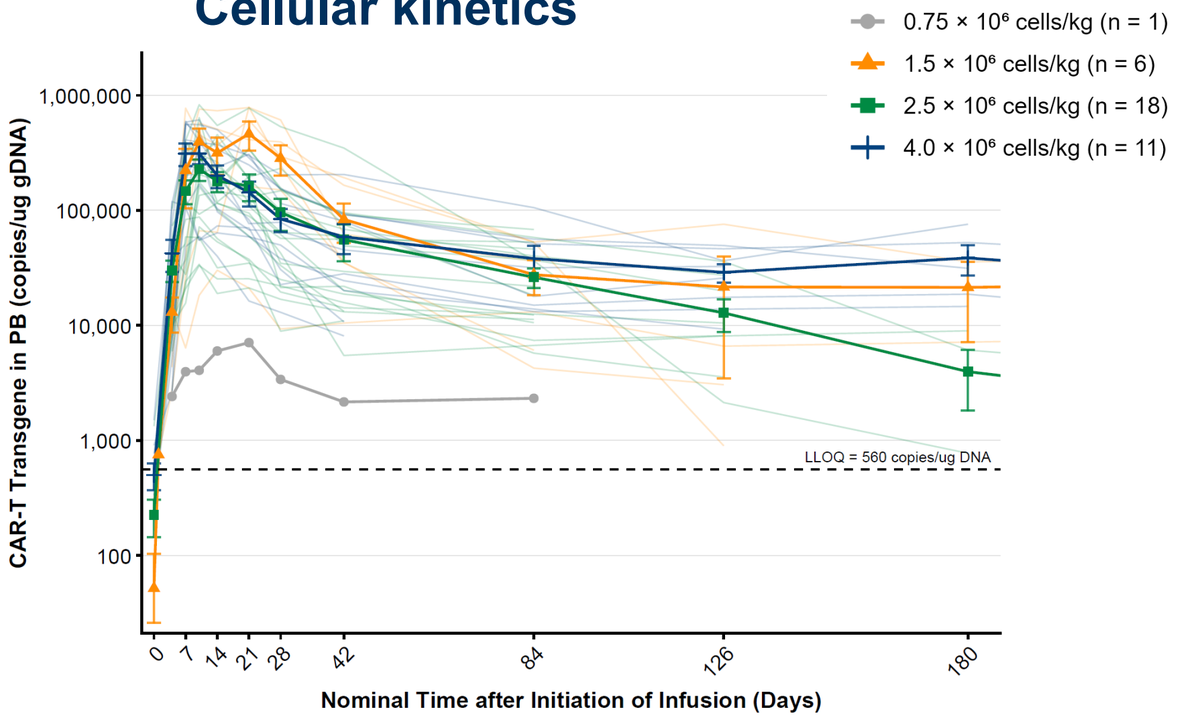
# AZD7003 showed rapid expansion and durable persistence with no DLTs

## Safety

- Most participants experienced Grade 1/2 CRS
  - Grade 3 CRS was reported in 2 participants (5.6%), both at the 4.0 × $10^6$ cells/kg dose level
- No ICANS or IEC-HS was observed
- ILD was reported in 2 participants (5.6%), both at the 4.0 × $10^6$ cells/kg dose level

Data cutoff 24 April 2026

## Cellular kinetics




- Rapid and consistent CAR T-cell expansion was observed across dose levels
- Median $T_{max}$ was achieved at 10 days (range: 7–31 days)
- Durable CAR T-cell persistence through month 6 was observed in 10/11 participants (91%)

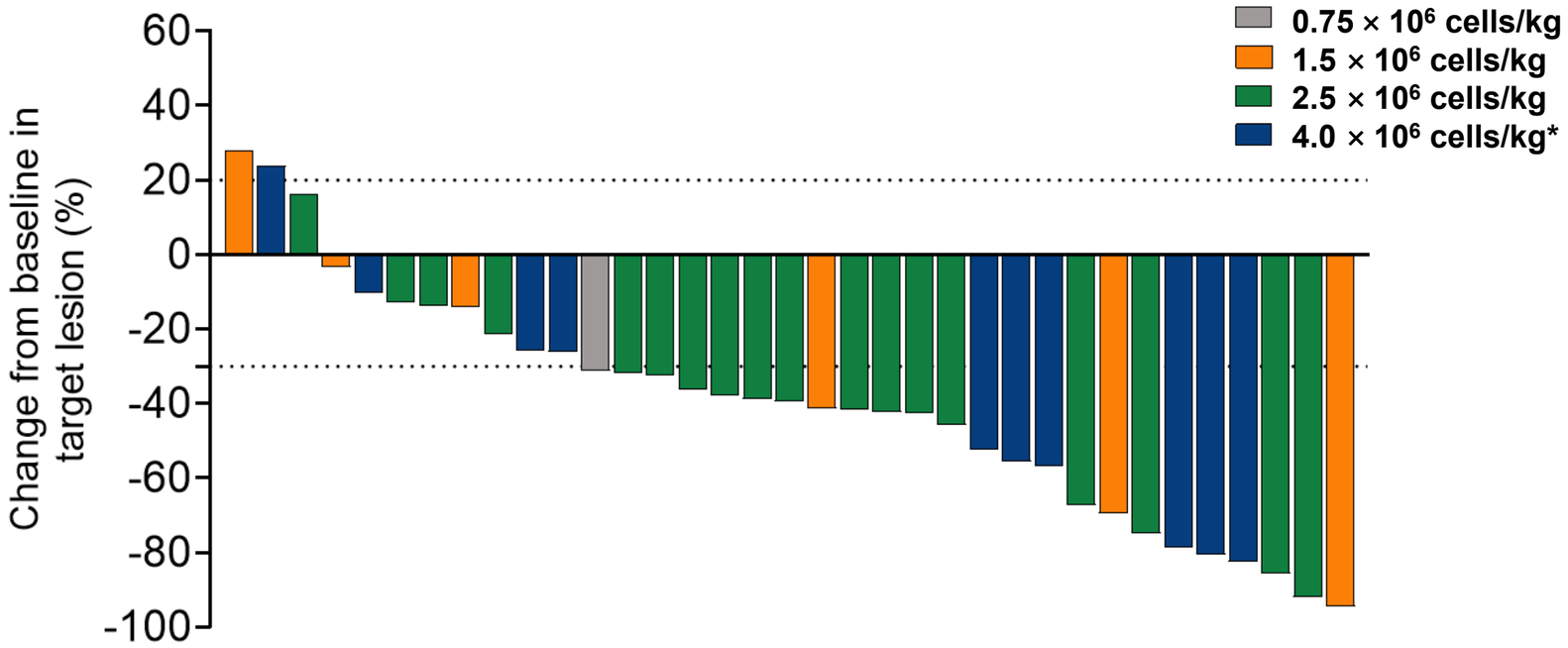
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CRS, cytokine release syndrome; gDNA, genomic DNA; ICANS, immune effector cell-associated neurotoxicity syndrome; IEC-HS, immune effector cell-associated haemophagocytic lymphohistiocytosis-like syndrome; ILD, interstitial lung disease; LLOQ, lower limit of quantification; PB, peripheral blood; Tmax, time to maximum observed concentration

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# Compelling response rate in a heavily pretreated patient population




| | 0.75 × $10^6$ cells/kg N=1 | 1.5 × $10^6$ cells/kg N=6 | 2.5 × $10^6$ cells/kg N=18 (RP2D†) | 4.0 × $10^6$ cells/kg N=11 | Overall N=36 |
|---|---|---|---|---|---|
| **ORR, n (%)** | 0 | 3 (50.0) | 7 (38.9) | 6 (54.5) | 16 (44.4) |
| **DCR, n (%)** | 1 (100) | 5 (83.3) | 18 (100) | 9 (81.8) | 33 (91.7) |

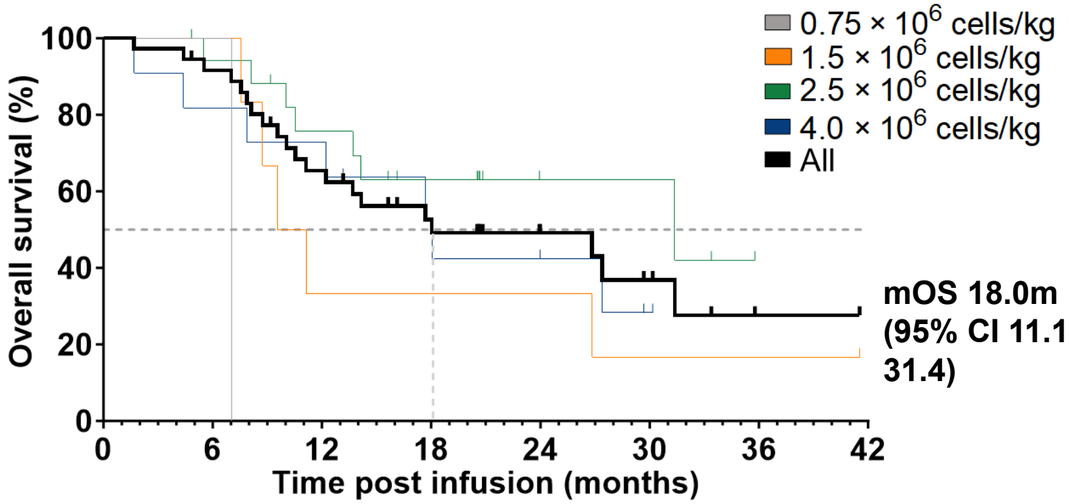
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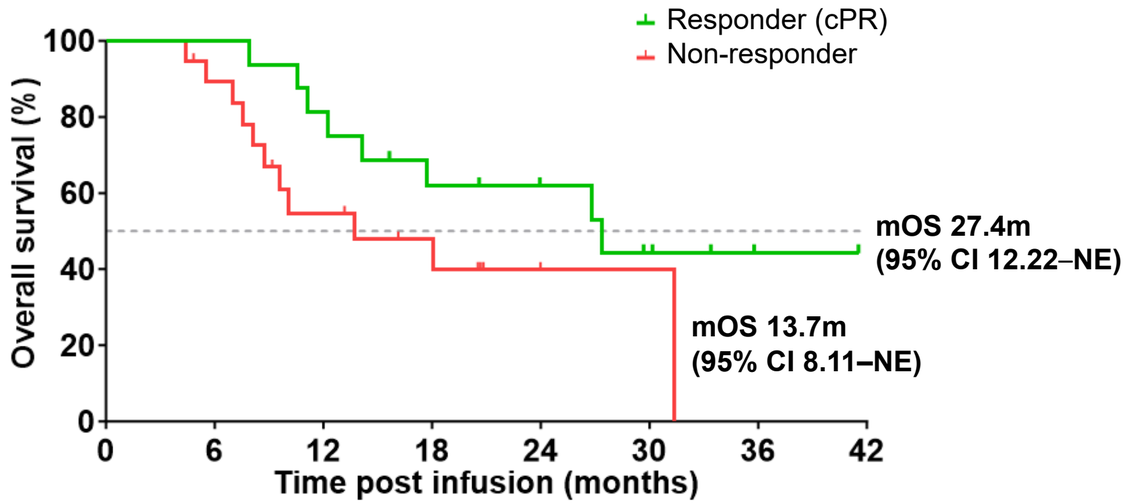
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*One participant excluded as no post-baseline tumor assessment available. †2.5 × 106 cells/kg was determined as the recommended phase 2 dose (RP2D) based on combined cellular kinetics, safety and efficacy data.

# Encouraging survival signal across dose levels, especially in responders




| Number at risk | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| 0.75 × 10^6 cells/kg | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| 1.5 × 10^6 cells/kg | 6 | 6 | 2 | 2 | 2 | 1 | 1 | 0 |
| 2.5 × 10^6 cells/kg | 18 | 16 | 12 | 8 | 3 | 3 | 0 | 0 |
| 4.0 × 10^6 cells/kg | 11 | 9 | 8 | 5 | 3 | 1 | 0 | 0 |
| All | 36 | 32 | 22 | 15 | 8 | 5 | 1 | 0 |




| Number at risk | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Responder | 16 | 16 | 13 | 9 | 7 | 4 | 1 | 1 |
| Non-responder* | 19 | 16 | 9 | 6 | 1 | 1 | 0 | 0 |

| | 0.75 × 10^6 cells/kg N=1 | 1.5 × 10^6 cells/kg N=6 | 2.5 × 10^6 cells/kg N=18 | 4.0 × 10^6 cells/kg N=11 | Overall N=36 |
|---|---|---|---|---|---|
| **12-month OS rate (95% CI)** | - | 33.3 (4.6, 67.6) | 75.6 (47.3, 90.1) | 72.7 (37.1, 90.3) | 65.4 (47.1, 78.7) |
| **Observed median follow-up time, month (Min, Max)** | 7.0 | 10.4 (7.6, 41.5) | 15.9 (4.8, 35.8) | 17.7 (1.7, 30.2) | 14.9 (1.7, 41.5) |

Data cutoff 15 August 2026

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*1 participant had no post-baseline tumour assessments and was not included in analysis
cPR, confirmed partial response; mOS, median overall survival; NE, not evaluable

# Conclusions

- In this FIH study in patients with HCC, AZD7003 had a tolerable safety profile with predominately Grade 1/2 CRS and no ICANS or IEC-HS
- AZD7003 showed rapid, robust expansion and long-term persistence in peripheral blood
- AZD7003 showed encouraging efficacy in heavily pretreated patients:
  - 44.4% ORR and 91.7% DCR across all dose levels
  - 65.4% 12-month OS rate (95% CI, 47.1–78.7)
- $2.5 \times 10^6$ cells/kg was determined as the recommended phase 2 dose
- These FIH results support further clinical development of AZD7003 in advanced HCC

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# Acknowledgements


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- The study can be found at *ClinicalTrials.gov* with identifier of NCT05155189


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