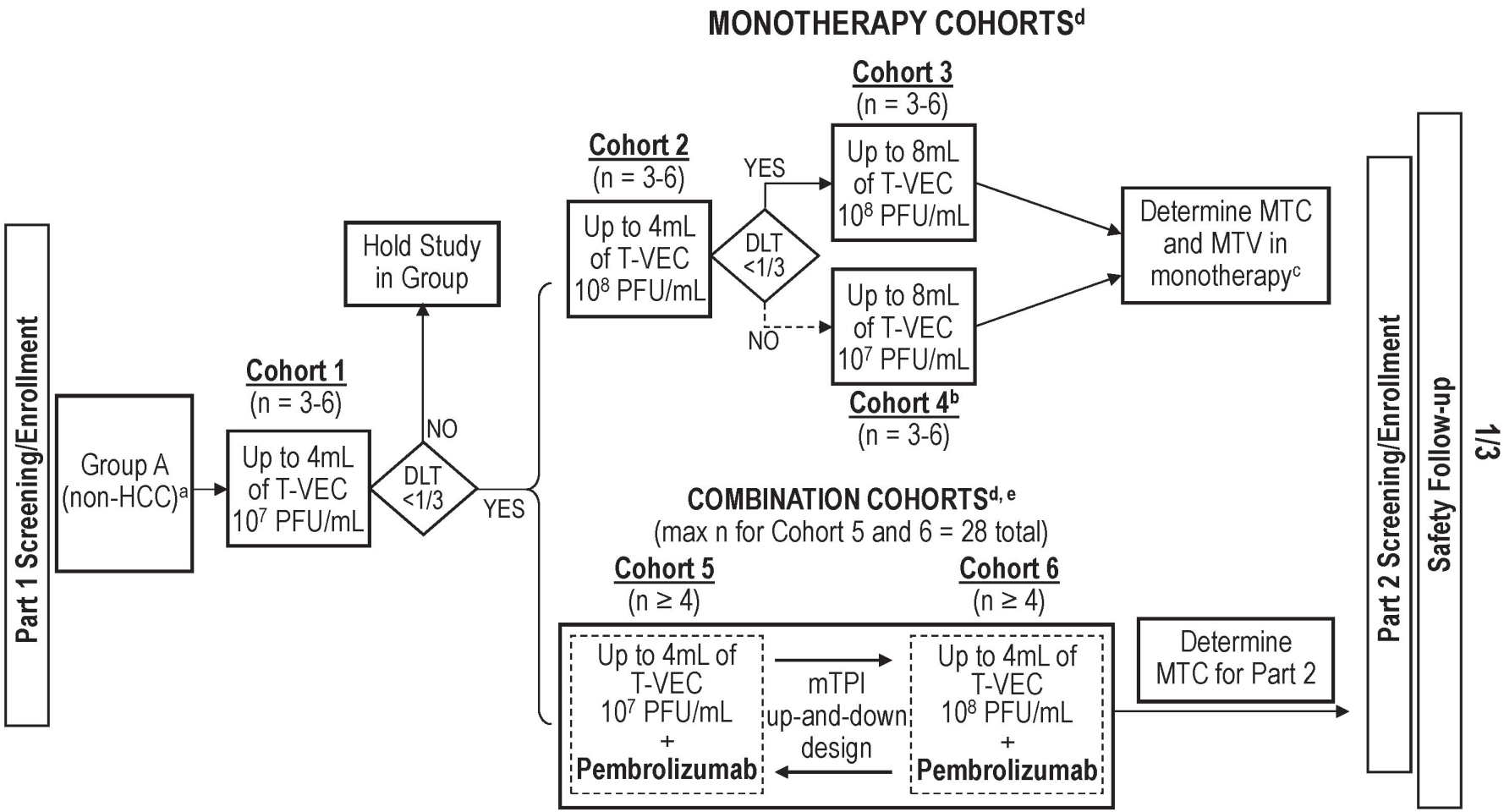

MONOTHERAPY COHORTS[d]
Cohort 3
(n = 3-6)
Cohort 2
(n = 3-6)
YES
Up to 8mL of T-VEC 10^8 PFU/mL
Up to 4mL of T-VEC 10^8 PFU/mL
DLT <1/3
Determine MTC and MTV in monotherapy[c]
Hold Study in Group
Cohort 1
(n = 3-6)
Group A (non-HCC)[a]
Up to 4mL of T-VEC 10^7 PFU/mL
DLT <1/3
NO
YES
NO
Up to 8mL of T-VEC 10^7 PFU/mL
Cohort 4[b]
(n = 3-6)
COMBINATION COHORTS[d, e]
(max n for Cohort 5 and 6 = 28 total)
Cohort 5
(n ≥ 4)
Cohort 6
(n ≥ 4)
Up to 4mL of T-VEC 10^7 PFU/mL + Pembrolizumab
mTPI up-and-down design
Up to 4mL of T-VEC 10^8 PFU/mL + Pembrolizumab
Determine MTC for Part 2
Part 1 Screening/Enrollment
Part 2 Screening/Enrollment
Safety Follow-up

Fig. 1

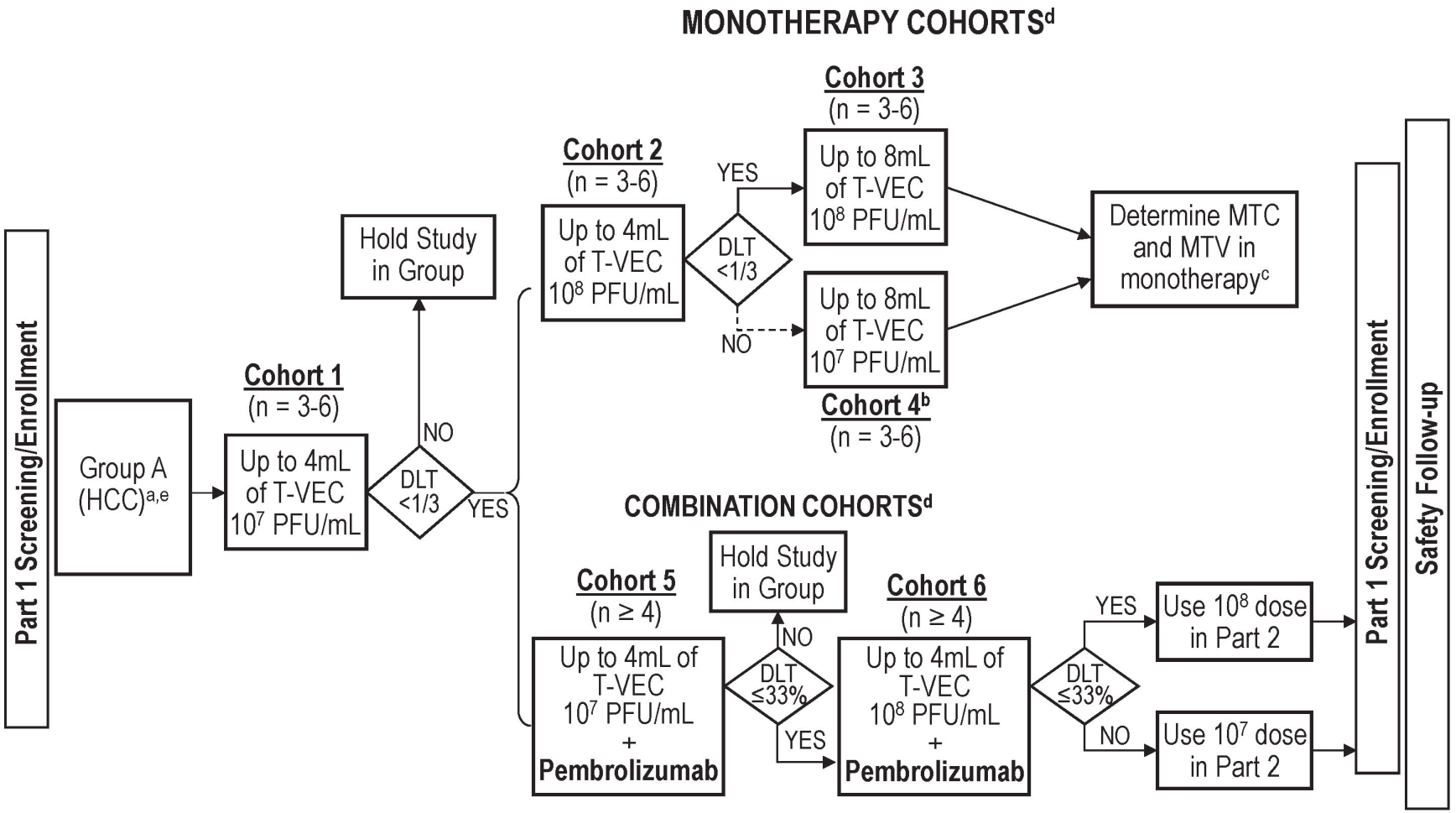

MONOTHERAPY COHORTS[d]
Part 1 Screening/Enrollment
Group A (HCC)[a,e]
Cohort 1 (n = 3-6)
Up to 4mL of T-VEC 10^7 PFU/mL
DLT <1/3
NO
Hold Study in Group
YES
Cohort 2 (n = 3-6)
Up to 4mL of T-VEC 10^8 PFU/mL
DLT <1/3
YES
Up to 8mL of T-VEC 10^8 PFU/mL
NO
Up to 8mL of T-VEC 10^7 PFU/mL
Cohort 3 (n = 3-6)
Cohort 4[b] (n = 3-6)
Determine MTC and MTV in monotherapy[c]
COMBINATION COHORTS[d]
Cohort 5 (n ≥ 4)
Up to 4mL of T-VEC 10^7 PFU/mL + Pembrolizumab
DLT ≤33%
NO
Hold Study in Group
YES
Cohort 6 (n ≥ 4)
Up to 4mL of T-VEC 10^8 PFU/mL + Pembrolizumab
DLT ≤33%
YES
Use 10^8 dose in Part 2
NO
Use 10^7 dose in Part 2
Part 1 Screening/Enrollment
Safety Follow-up
2/3

Fig. 2

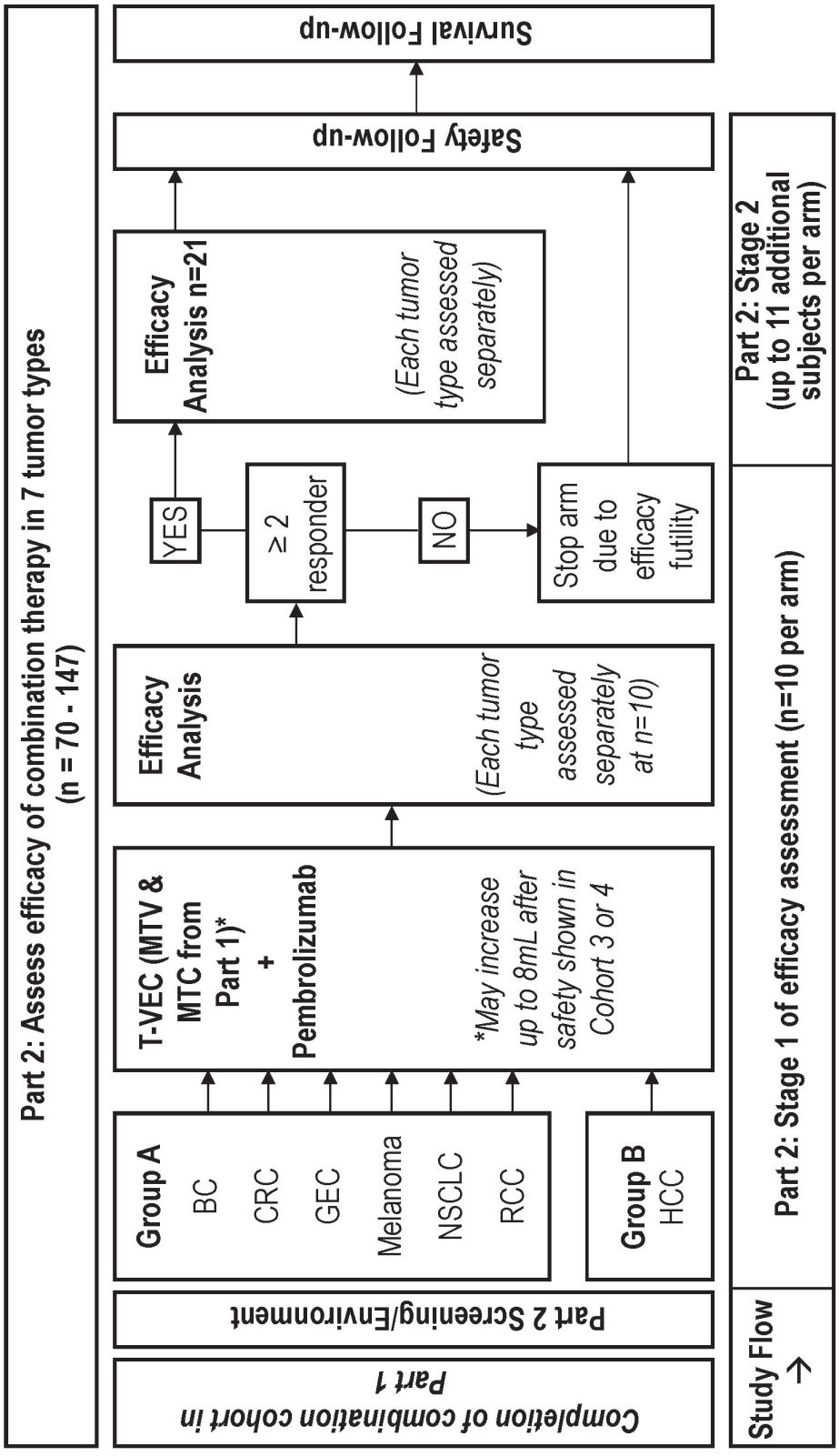

Part 2: Assess efficacy of combination therapy in 7 tumor types
(n = 70 - 147)
Completion of combination cohort in Part 1
Part 2 Screening/Environment
Group A
BC
CRC
GEC
Melanoma
NSCLC
RCC
Group B
HCC
T-VEC (MTV & MTC from Part 1)* + Pembrolizumab
*May increase up to 8mL after safety shown in Cohort 3 or 4
Efficacy Analysis
(Each tumor type assessed separately at n=10)
≥ 2 responder
YES
NO
Stop arm due to efficacy futility
Efficacy Analysis n=21
(Each tumor type assessed separately)
Safety Follow-up
Survival Follow-up
Study Flow →
Part 2: Stage 1 of efficacy assessment (n=10 per arm)
Part 2: Stage 2 (up to 11 additional subjects per arm)

Fig. 3