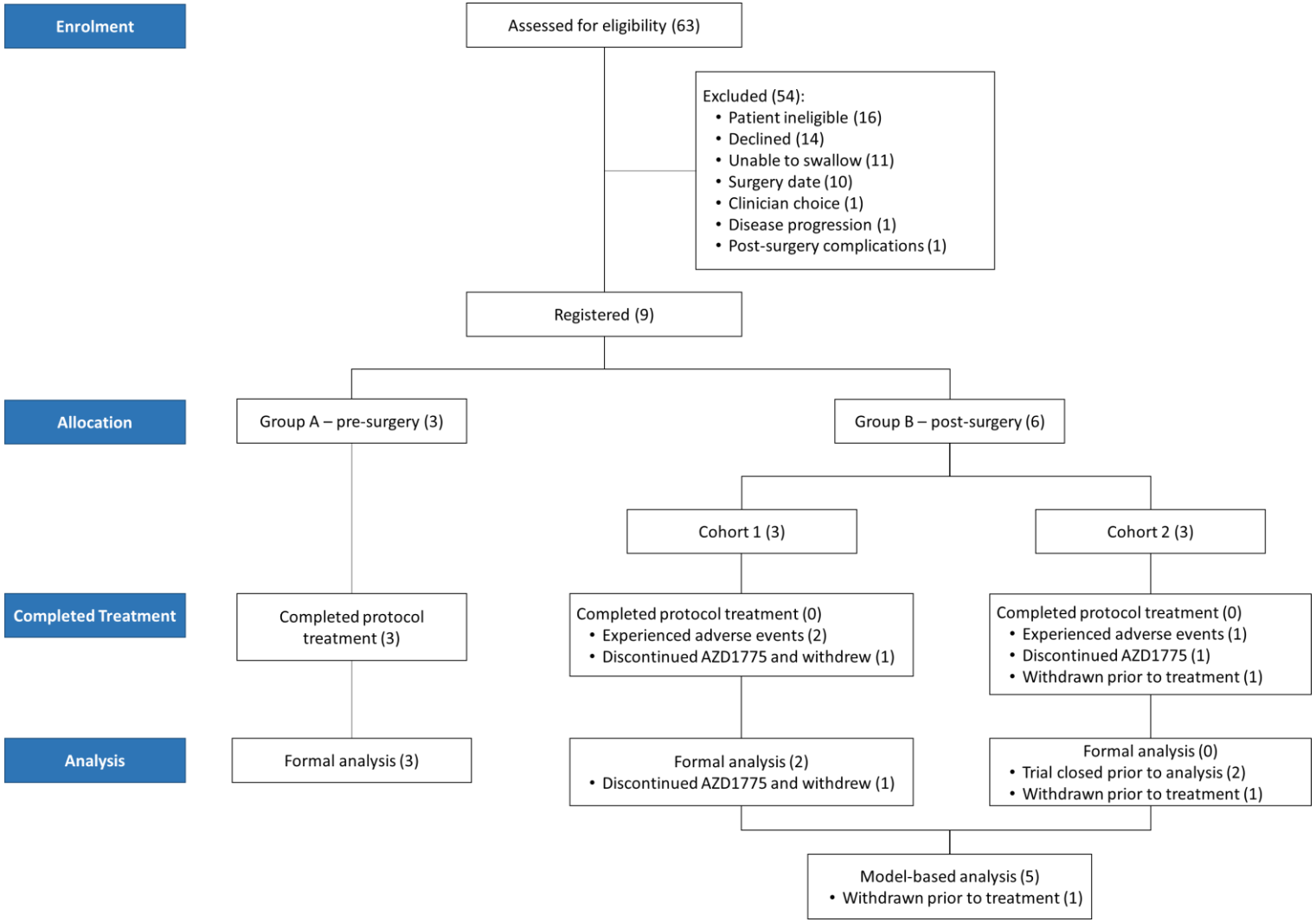
1. Participant Flow



2. Baseline Characteristics

Table 1: Baseline Characteristics

Characteristic		Treatment Group		
		Group A – Pre-surgery	Group B – Post-surgery	Overall
Sex (N)				
	Male	1	4	5
	Female	2	2	4
	Total	3	3	9
Age (years)				
	N	3	6	9
	Mean (sd)	52.3 (4.2)	61.0 (2.3)	58.1 (5.1)
	Median	51.0	61.0	59.0
	IQR	49.0, 57.0	59.0, 63.0	57.0, 61.0
	Range	49.0, 57.0	58.0, 64.0	49.0, 64.0
ECOG (N)				
	0	3	4	7
	1	0	2	2
	Total	3	6	9
Histology (N)				
	Squamous cell carcinoma	3	6	9
	Total	3	6	9
Tumour Types (N)				
	Oral cavity	3	4	7
	Hypopharynx larynx	0	1	1
	Larynx	0	1	1
	Total	3	6	9
Side of Tumour (N)				
	Left	2	4	6
	Right	1	2	3
	Total	3	6	9
Tumour Differentiation (N)				
	Moderate	3	5	8
	Poor	0	1	1
	Total	3	6	9

Characteristic	Treatment Group		Overall
	Group A – Pre-surgery	Group B – Post-surgery	
Smoking Status (N)			
Current smoker	1	3	4
Ex-smoker	1	1	2
Never smoked	1	2	3
Total	3	6	9
Alcohol Status (N)			
Never drank	0	1	1
Previous drinker	0	2	2
Current	3	3	6
Total	3	6	9

3. Outcome Measures

3.1 Primary Outcome

3.1.1 Dose Limiting Toxicity Assessment for Group A – Cohort 1

Table 2: Per patient treatment doses, number of observed DLTs and proportion of DLT assessment period completed.

Cohort	Dose Level	DLT	Proportion of DLT Assessment Period
1	0	0	1 (42/42)
1	0	0	1 (42/42)
1	0	0	1 (42/42)

Each row of the table represents an individual patient.

Table 3: Group A dose levels, prior and posterior probabilities of DLTS for each dose level with associated 90% credible intervals, based on the modified TITE-CRM dose-toxicity model.

Dose Level	AZD1775 Dose (mg)	Prior DLT Rate	No. of Evaluable Patients	No. of DLTs	Posterior DLT Rate (90% credible interval)
-1	75	0.02	0	0	0.003 (0-0.203)
0 (starting dose)	100	0.06	3	0	0.014 (0-0.317)
1	125	0.14	0	0	0.050 (0-0.448)
2	150	0.25	0	0	0.120 (0-0.568)

3.1.2 Dose Limiting Toxicity Assessment for Group B – Cohorts 1 and 2

Table 4: Per patient treatment doses, number of observed DLTs and proportion of DLT assessment period completed.

Cohort	Dose Level	DLT	Proportion of DLT Assessment Period
1	0	1	1
1	0	1	1
1	0	0	0.607 (51/84)
2	0	1	1
2	-	-	-
2	0	1	1

Each row of the table represents an individual patient.

Table 5: Group B dose levels, prior and posterior probabilities of DLTS for each dose level with associated 90% credible intervals, based on the modified TITE-CRM dose-toxicity model

Dose Level	AZD1775 Dose (mg)	Prior DLT Rate	No. of Evaluable Patients	No. of DLTs	Posterior DLT Rate (90% credible interval)
-1	50	0.12	0	0	0.525 (0.179-0.786)
0 (starting dose)	75	0.20	5	4	0.646 (0.310-0.849)
1	100	0.30	0	0	0.747 (0.458-0.897)
2	125	0.40	0	0	0.820 (0.588-0.929)

3.2 Secondary Outcomes

3.2.1 Disease-free Survival – Group A

Table 6: Group A Disease-free survival

Registration Date	4 Week Follow Up Date	4 Week Patient Status	4 Week Follow Up No Disease	12 Week Follow Up Date	12 Week Patient Status	12 Week Follow Up No Disease
30-Oct-2017	12-Dec-2017	Alive	Yes	8-Feb-2018	Alive	Yes
20-Nov-2017	17-Jan-2018	Alive	Yes	27-Feb-2018	Alive	Yes
12-Mar-2018	24-Apr-2018	Alive	Yes	20-Jun-2018	Alive	Yes

Each row of the table represents an individual patient.

3.2.2 Disease-free Survival – Group B

Table 7: Group B Disease-free survival

Registration Date	4 Week Follow Up Date	4 Week Patient Status	4 Week Follow Up No Disease	12 Week Follow Up Date	12 Week Patient Status	12 Week Follow Up No Disease
29-Nov-2017	5-Jun-2018	Alive	Yes	4-Dec-2018	Alive	Yes
8-Jun-2018	21-Jan-2019	Alive	Yes	8-Jul-2019	Alive	Yes
6-Nov-2018	13-May-2019	Alive	Yes	11-Nov-2019	Alive	Yes
18-Jan-2019	9-Jul-2019	Alive	Yes	7-Jan-2020	Alive	Yes
15-Jul-2019	29-Jan-2020	Alive	Yes	3-Aug-2020	Alive	Yes

Each row of the table represents an individual patient.

3.3 Tertiary Outcomes

- **Pharmacodynamic (PD) Effects of AZD1775 & Correlation with TP53 Mutation Status**
  Due to the early stopping of the trial, the data required for assessing the pharmacodynamic effects of AZD1175 was unavailable.
- **Pharmacokinetic (PK) Effects of AZD1775**
  Due to the early stopping of the trial, the data required for assessing the pharmacokinetic effects of AZD1175 was unavailable.
- **Optimise, validate and test feasibility of assays to investigate serum, ctDNA and RNA biomarkers**

  Due to the early stopping of the trial, the data required for assessing feasibility of assays to investigate serum, ctDNA and RNA biomarkers was unavailable.
- **Investigate the feasibility of immune function testing in a multicentre setting**

  Due to the early stopping of the trial, the data required for investigating the feasibility of immune function testing in a multicentre setting was unavailable.
- **Complete Pathological Response Rate for Group A**
  No resection pathology details were collected.
- **Positive Resection Margin Status in Group A**
  Resection margin information was unavailable.
- **Surgical Complication in Group A**
  Surgical complications data were unavailable.
- **Quality of Life in Group B**
  Quality of Life questionnaires were completed by patients recruited into Group B and contained questions from EORCT QLQ (European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire) C30 (version 3.0), EORCT QLQ H&N35 and MDADI (MD Anderson Dysphagia Inventory).

  The descriptive statistics were obtained for each question category at each data collection time-point and tabulated but are not provided with this report.

4. Adverse Events

Table 8: Adverse events by CTCAE v4.0 category and grade

	CTCAE Grade				
Adverse Event Category (N (%))	**Grade 1**	**Grade 2**	**Grade 3**	**Grade 4**	**Overall**
Group A					
Blood and lymphatic system disorders	0 (0.0)	0 (0.0)	3 (30.0)	0 (0.0)	3 (6.8)
Cardiac disorders	1 (7.1)	1 (5.0)	0 (0.0)	0 (0.0)	2 (4.5)
Gastrointestinal disorders	6 (42.9)	11 (55.0)	1 (10.0)	0 (0.0)	18 (40.9)
General disorders and administration site conditions	1 (7.1)	2 (10.0)	0 (0.0)	0 (0.0)	3 (6.8)
Infections and infestations	0 (0.0)	2 (10.0)	0 (0.0)	0 (0.0)	2 (4.5)
Injury, poisoning and procedural complications	1 (7.1)	2 (10.0)	0 (0.0)	0 (0.0)	3 (6.8)
Investigations	1 (7.1)	0 (0.0)	2 (20.0)	0 (0.0)	3 (6.8)
Metabolism and nutrition disorders	2 (14.3)	0 (0.0)	4 (40.0)	0 (0.0)	6 (13.6)
Nervous system disorders	1 (7.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.3)
Psychiatric disorders	1 (7.1)	1 (5.0)	0 (0.0)	0 (0.0)	2 (4.5)
Respiratory, thoracic and mediastinal disorders	0 (0.0)	1 (5.0)	0 (0.0)	0 (0.0)	1 (2.3)
Total	**14**	**20**	**10**	**0**	**44**
Group B					
Blood and lymphatic system disorders	3 (4.8)	5 (10.6)	2 (9.5)	1 (100.0)	11 (8.3)
Ear and labyrinth disorders	1 (1.6)	1 (2.1)	0 (0.0)	0 (0.0)	2 (1.5)
Gastrointestinal disorders	27 (42.9)	20 (42.6)	5 (23.8)	0 (0.0)	52 (39.4)
General disorders and administration site conditions	6 (9.5)	5 (10.6)	1 (4.8)	0 (0.0)	12 (9.1)
Infections and infestations	0 (0.0)	1 (2.1)	0 (0.0)	0 (0.0)	1 (0.8)
Injury, poisoning and procedural complications	3 (4.8)	2 (4.3)	1 (4.8)	0 (0.0)	6 (4.5)
Investigations	1 (1.6)	2 (4.3)	4 (19.0)	0 (0.0)	7 (5.3)
Metabolism and nutrition disorders	10 (15.9)	4 (8.5)	6 (28.6)	0 (0.0)	20 (15.2)
Musculoskeletal and connective tissue disorders	1 (1.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)
Nervous system disorders	4 (6.3)	4 (8.5)	0 (0.0)	0 (0.0)	8 (6.1)
Psychiatric disorders	0 (0.0)	1 (2.1)	0 (0.0)	0 (0.0)	1 (0.8)
Respiratory, thoracic and mediastinal disorders	1 (1.6)	1 (2.1)	0 (0.0)	0 (0.0)	2 (1.5)
Skin and subcutaneous tissue disorders	5 (7.9)	1 (2.1)	2 (9.5)	0 (0.0)	8 (6.1)
Surgical and medical procedures	1 (1.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)
Total	**63**	**47**	**21**	**1**	**132**

Table 9: Serious Adverse Events category, outcome and expectedness information by treatment group

	Treatment Group		
	Group A	**Group B**	**Overall**
Serious Adverse Event Category (N (%))			
Unrelated SAE	2	1 (20.0)	3 (42.9)
SAR	0 (0.0)	3 (60.0)	3 (42.9)
Non-fatal/life-threatening SUSAR	0 (0.0)	1 (20.0)	1 (14.3)
Total	**2**	**5**	**7**
Outcome (N (%))			
Resolved – no sequelae	0 (0.0)	4 (80.0)	4 (57.1)
Resolved – with sequelae	2 (100.0)	1 (20.0)	3 (42.9)
Total	**2**	**5**	**7**
Expectedness (N (%))			
No	2 (100.0)	5 (100.0)	7 (100.0)
Total	**2**	**5**	**7**