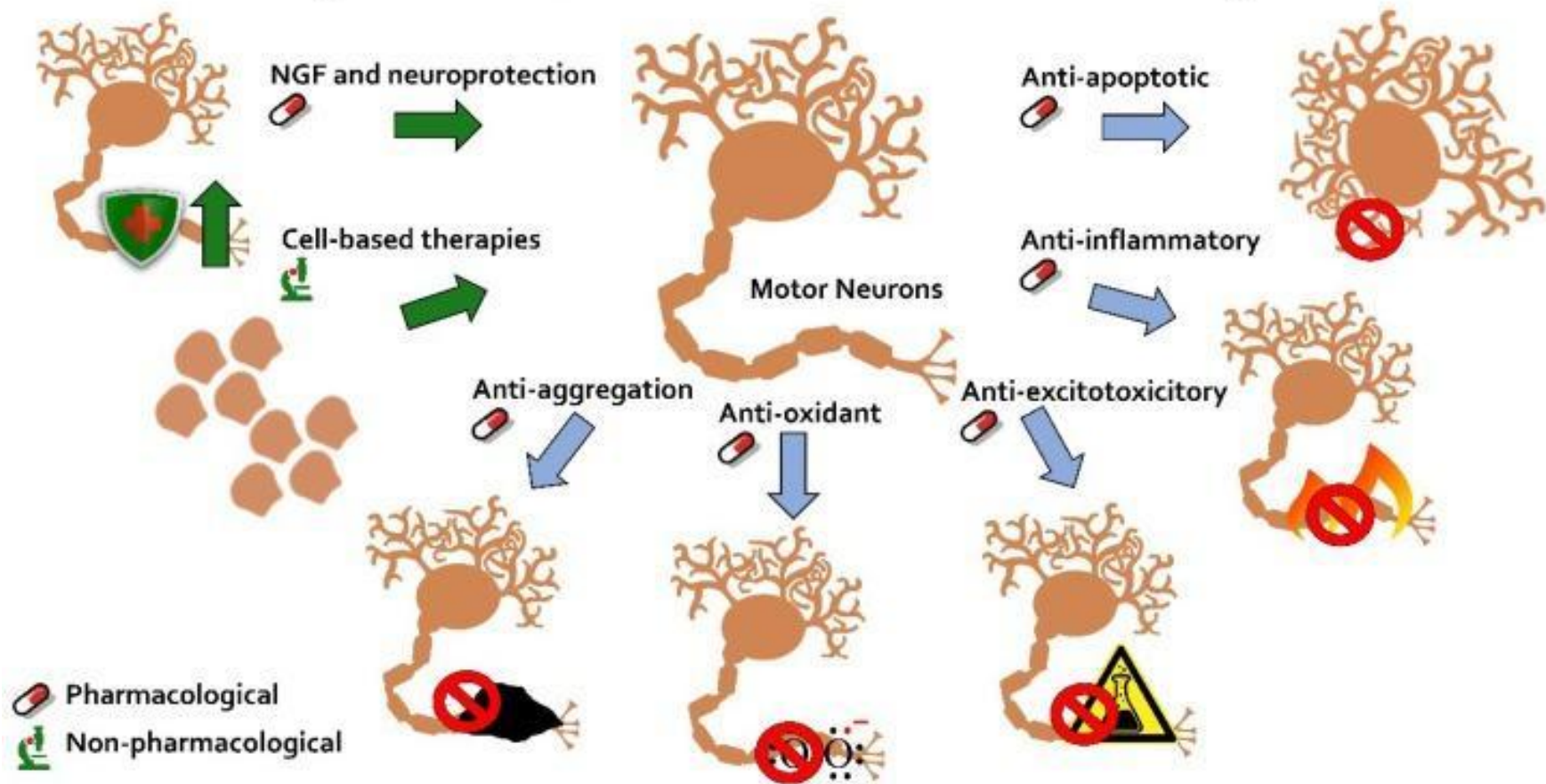




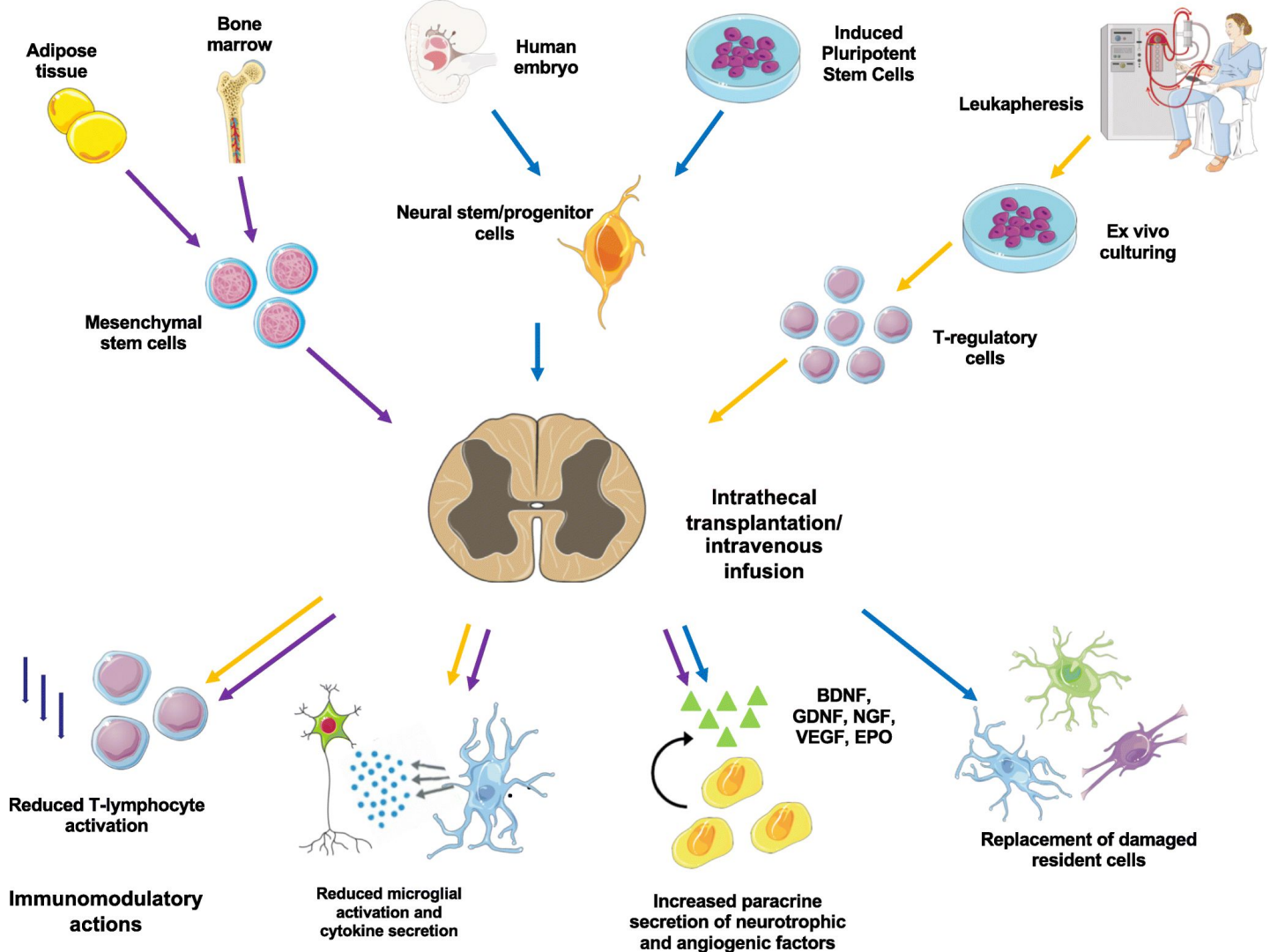
Возможности лечения БАС на современном этапе. Прогноз

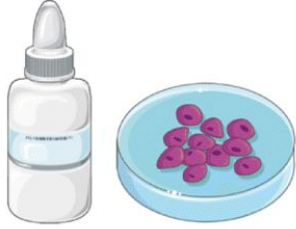
Доклад подготовил:
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Зевахин С.В.

General Approaches in ALS Treatment Research



Compound	Route	Primary endpoint/s	Phase/s	Outcome	Funding [§]	Reference
Anti-glutamatergic						
Ceftriaxone	i.v.	ALSFRS-R; DTP	1–2; 3	Failure	Academic	Berry et al., 2013; Cudkowicz M. et al., 2013
Memantine	Oral	ALSFRS	2–3	Failure	Academic	de Carvalho et al., 2010
Riluzole	Oral	Survival	3	Mixed*	Mixed	Bensimon et al., 1994, 2002; Lacomblez et al., 1996
Talampanel	Oral	ALSFRS-R	2	Failure	Industry	Pascuzzi et al., 2010; Teva, 2010
Anti-inflammatory						
Celecoxib	Oral	MVIC	2–3	Failure	Industry	Cudkowicz et al., 2006
Erythropoietin	i.v.	DTP	2; 3	Failure	Academic	Lauria et al., 2009, 2015
Glatiramer acetate	s.c.	ALSFRS-R	2; 2–3	Failure	Industry	Gordon et al., 2006; Meininger et al., 2009
Minocycline	Oral	ALSFRS-R	1–2; 3	Failure	Academic	Gordon et al., 2004, 2007; Pontieri et al., 2005
NP001	i.v. infusion	ALSFRS-R	1; 2	Failure	Industry	Miller et al., 2014, 2015
Pioglitazone	Oral	Survival	2	Failure	Industry	Dupuis et al., 2012
Valproic acid	Oral	DTP	3	Failure	Academic	Piepers et al., 2009
Anti-oxidative						
Coenzyme Q10	Oral	ALSFRS-R	2	Failure	Academic	Ferrante et al., 2005; Kaufmann et al., 2009
Creatine	Oral	DTP; MVIC	2; 2–3; 3	Failure	Academic	Rosenfeld, 2001; Groeneveld et al., 2003; Shefner et al., 2004; Rosenfeld et al., 2008; Pastula et al., 2012
Edaravone	i.v. infusion	ALSFRS-R	2; 3	Mixed**	Industry	Yoshino and Kimura, 2006; Abe et al., 2014; Palumbo et al., 2016; Sakata et al., 2016; Tanaka et al., 2016a,b
Neuroprotective						
Dexpramipexole	Oral	CAFS	2; 3	Failure	Industry	Cudkowicz et al., 2011; Cudkowicz M. E. et al., 2013; Bozik et al., 2014
Olesoxime	Oral	Survival	2–3	Failure	Mixed	Lenglet et al., 2014
TCH346	Oral	ALSFRS-R	2–3	Failure	Industry	Miller et al., 2007a
Xaliproden	Oral	MMT; DTP	2; 3	Failure	Industry	Lacomblez et al., 2004; Meininger et al., 2004
Neurotrophic factors						
BDNF	i.v.	Survival; %FVC	1–2; 3	Failure	Mixed	Bradley, 1995; Kasarskis et al., 1999
CNTF	s.c.	MVIC	1; 1–2; 2–3; 3	Failure	Mixed	Miller et al., 1993, 1996; ALS CNTF Treatment Study Group, 1995, 1996
IGF-1	s.c.	AALS; MMT	3	Failure	Mixed	Lai et al., 1997; Borasio et al., 1998; Sorenson et al., 2008
CSF1R inhibition						
Masitinib	Oral	ALSFRS-R	2–3	Positive [§]	Industry	
Other						
Lithium	Oral	ALSFRS-R; Survival	2; 2–3; 3	Failure [£]	Mixed	Fornai et al., 2008; Aggarwal et al., 2010; Verstraete et al., 2012; Morrison et al., 2013
Tirasemtiv	Oral	ALSFRS-R	2	Failure	Industry	Shefner et al., 2012, 2013a,b, 2016

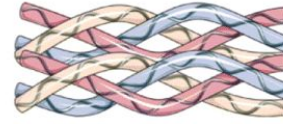




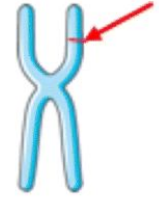
Pharmacologic preconditioning



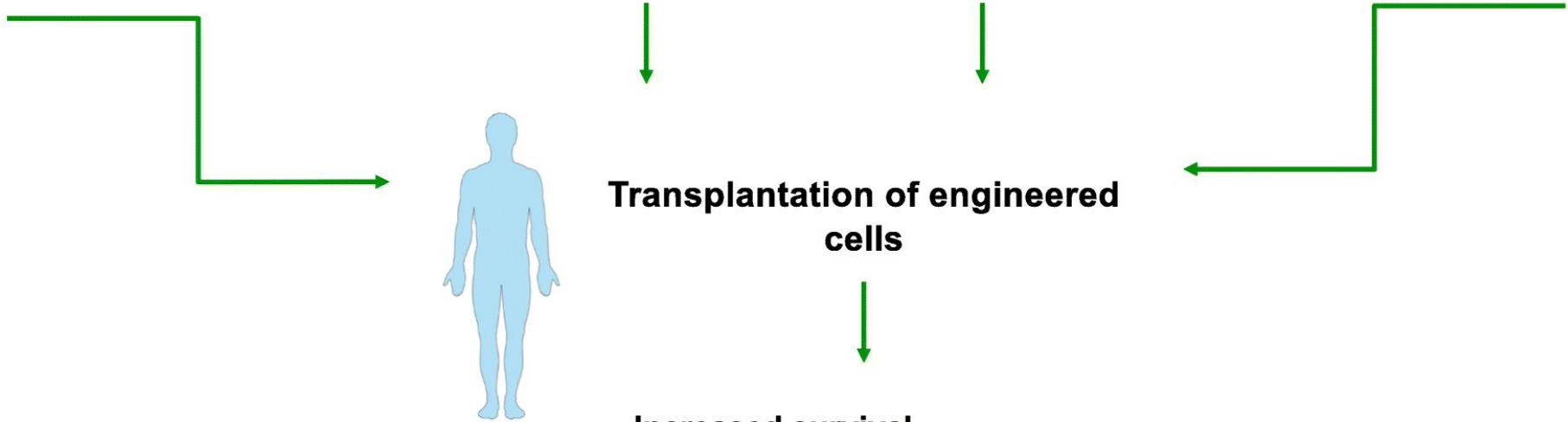
Hypoxic preconditioning



Hydrogel scaffold

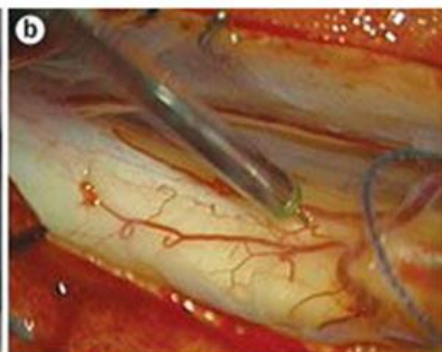
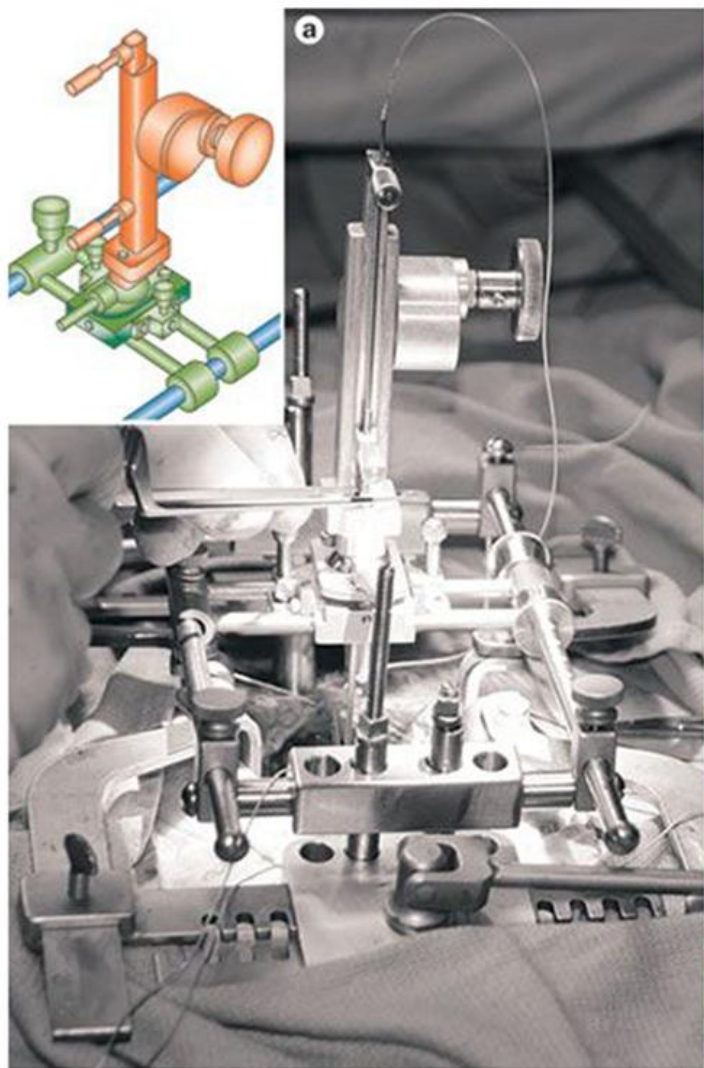


Genetic engineering



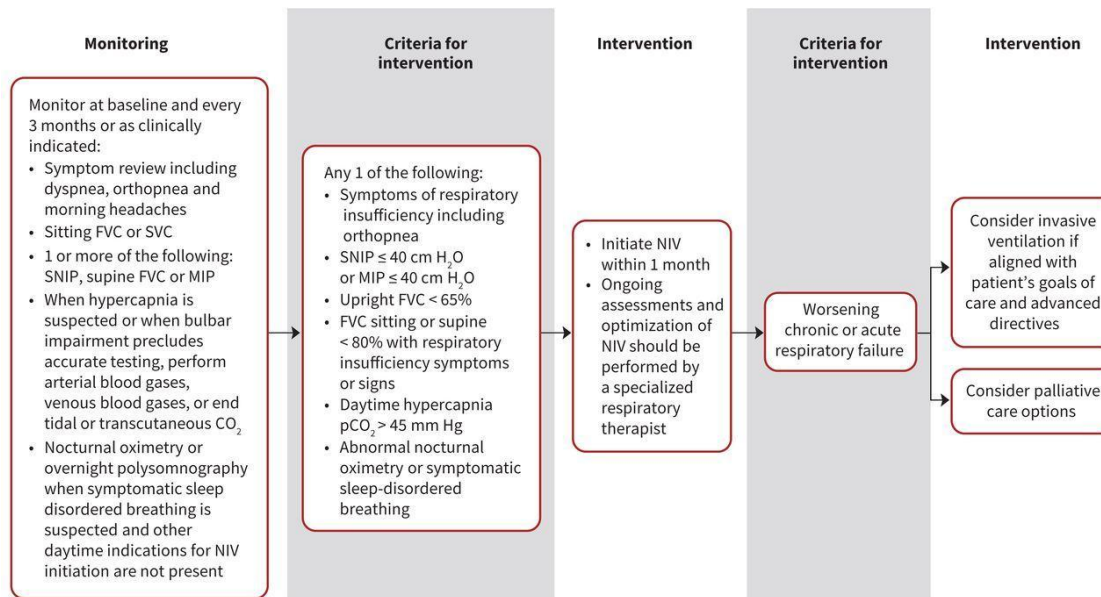
Transplantation of engineered cells

- **Increased survival**
- **Enhanced growth factors secretion**
- **Increased neuroprotective properties**
- **Increased expression of anti-apoptotic, anti-oxidant and trophic genes**

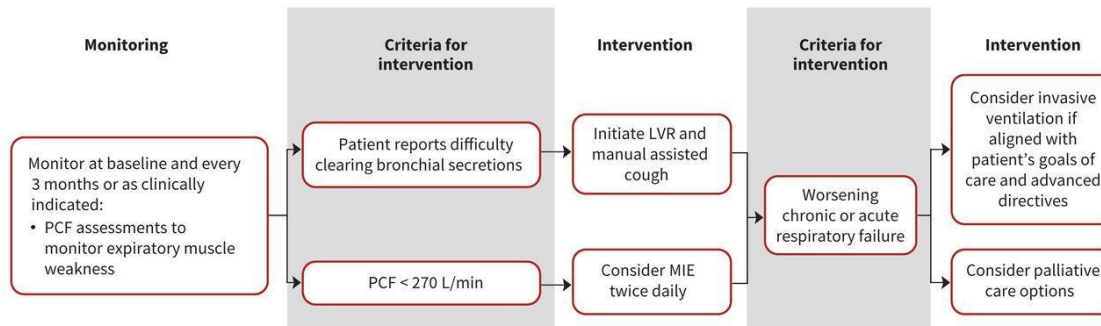


Cell source	Dose	Mode and site of delivery	Number of patients	Follow-up (months)	Adverse events	Refs.
Autologous bone marrow	$1 \times 10^6/\text{kg} \times 2$ doses	Lumbar intrathecal infusion	8 enrolled, 7 treated	12	Flu-like illness (62.5%), back pain (50%), headache (25%)	Oh et al. [44]
Autologous bone marrow	Phase 1/2: $1 \times 10^6/\text{kg}$ Phase 2a: $1 \times 10^6/\text{kg}$, $1.5 \times 10^6/\text{kg}$, $2 \times 10^6/\text{kg}$	Lumbar intrathecal infusion \pm intramuscular injection	Phase 1/2: 6 intrathecal, 6 intramuscular Phase 2a: 14 intrathecal + intramuscular	6	Headache (50%) Fever (42%) Back pain (30%)	Petrou et al. [46]
Autologous adipose tissue	Escalating 1×10^7 to $1 \times 10^8 \times 2$ monthly infusions	Lumbar intrathecal infusion	27 enrolled and treated	24	Dose-dependent lumbosacral polyradiculitis (80% of patients receiving the highest dose)	Staff et al. [43]
Autologous bone marrow	$1.5 \pm 4.5 \times 10^7$	Lumbar intrathecal infusion	26 enrolled and treated	12	Headache (30%)	Sykova et al. [47]

A) Ventilation



B) Airway clearance



Monitoring

Monitor weight and BMI every 3 months or as clinically indicated; consider TDEE

Monitor swallowing safety regularly by a certified swallowing clinician using objective measures (MBS or FEES)

Monitor respiratory status at baseline and every 3 months or as clinically indicated

Criteria for intervention

- 5%–10% reduction in weight from usual or baseline weight
- 1-point reduction in BMI from usual or baseline BMI
- BMI < 18.5, or
- TDEE exceeds daily intake

Unsafe swallowing according to objective measures (MBS or FEES)

Decrease in FVC approaching 50%

FVC < 50%

Intervention

- Consider high-calorie diets
- Consider enteral feeding tube insertion (RIG or PEG)

- Consider enteral feeding tube insertion (RIG or PEG)
- Consider parenteral nutrition if enteral nutrition unsuccessful
- NG feeding if no other procedure is possible

Consider enteral feeding tube insertion (RIG or PEG)

Consider enteral feeding tube insertion (RIG or PEG); carefully monitor respiratory status during and after procedure