Возможности лечения БАС на современном этапе. Прогноз

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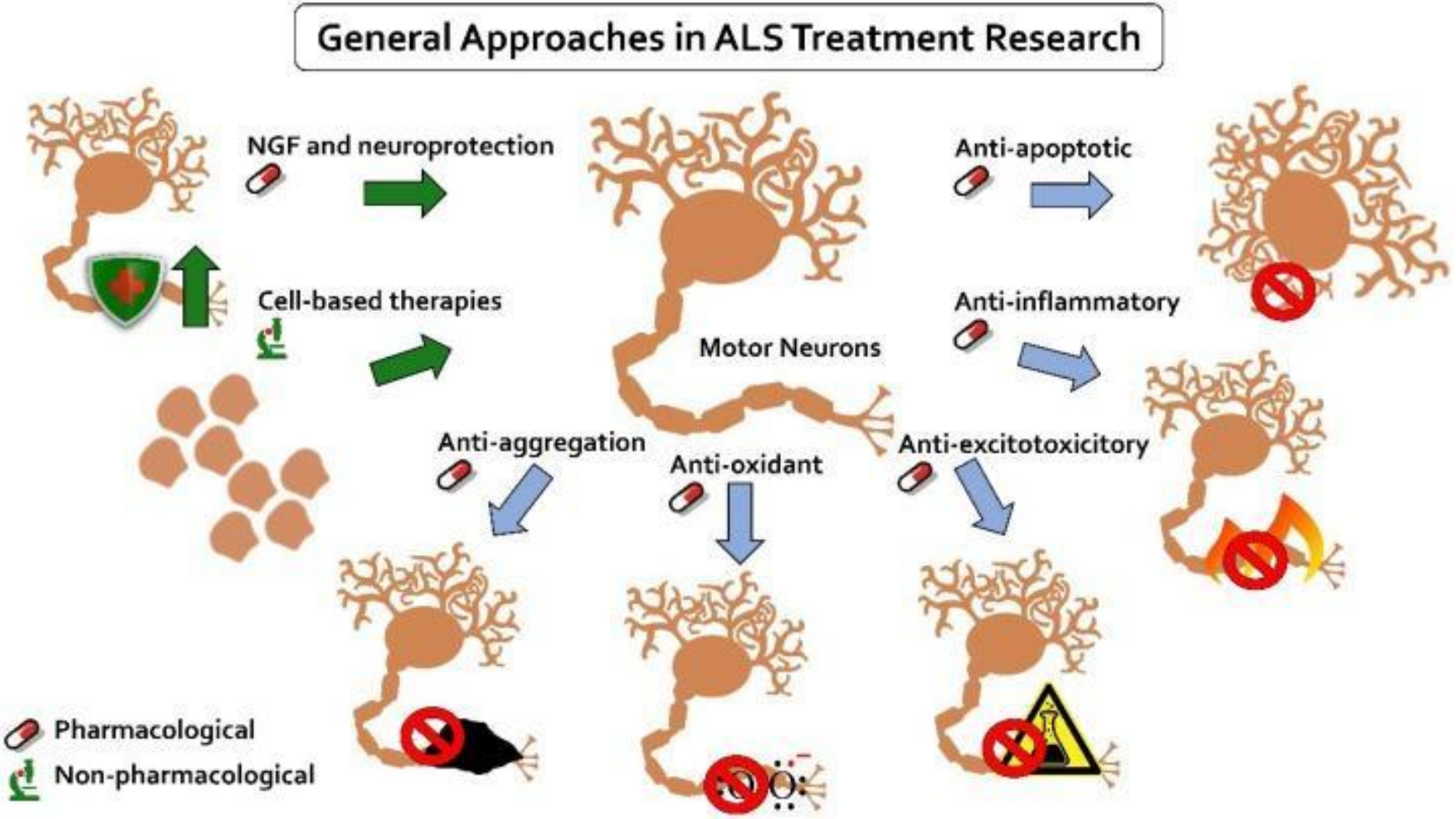
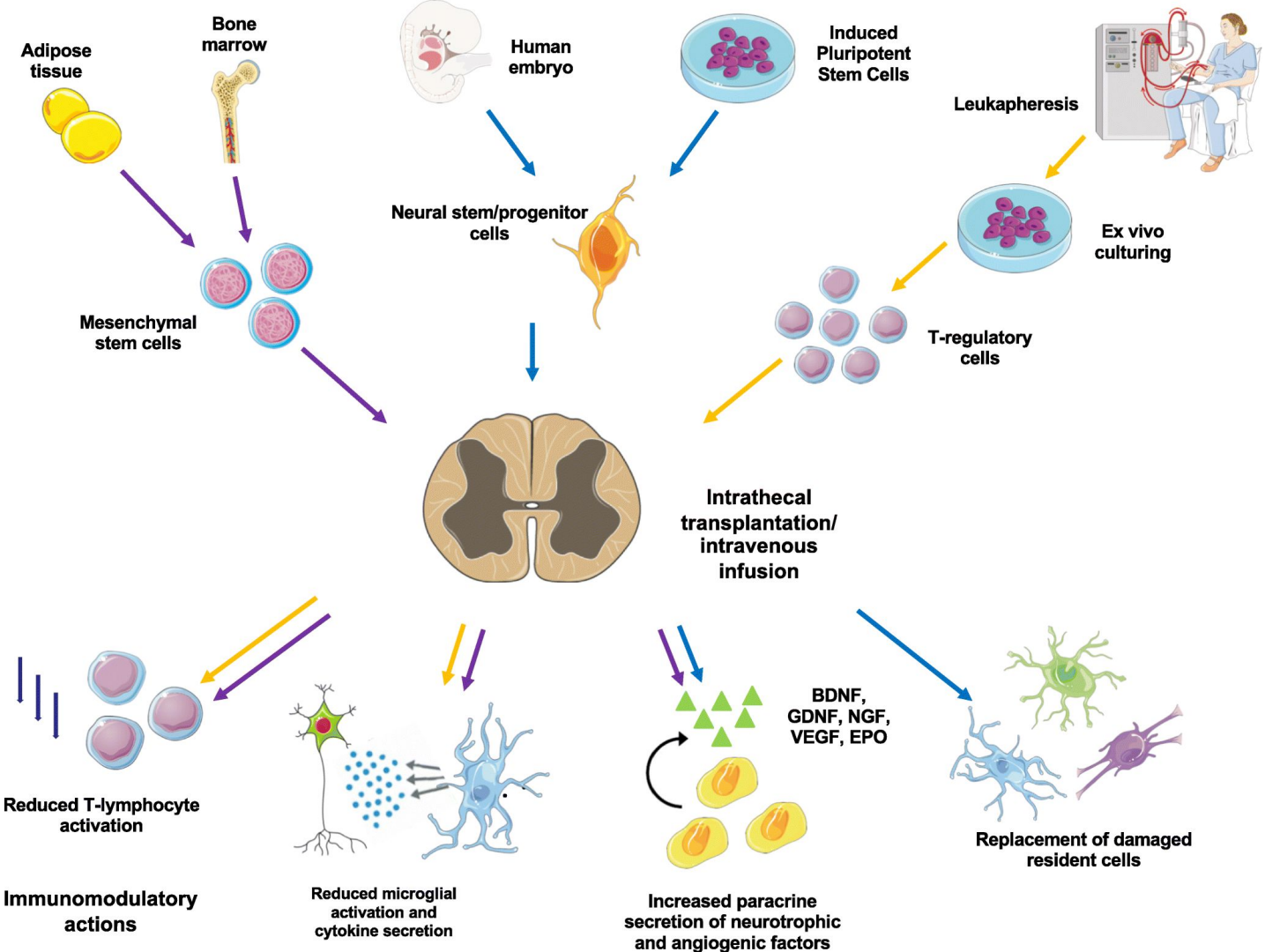
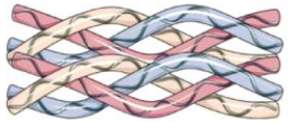

General Approaches in ALS Treatment Research
NGF and neuroprotection
Anti-apoptotic
Cell-based therapies
Anti-inflammatory
Motor Neurons
Anti-aggregation
Anti-oxidant
Anti-excitotoxicitory
Pharmacological
Non-pharmacological

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

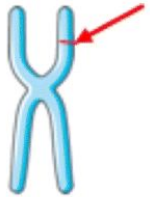

Adipose tissue
Bone marrow
Human embryo
Induced Pluripotent Stem Cells
Leukapheresis
Neural stem/progenitor cells
Ex vivo culturing
Mesenchymal stem cells
T-regulatory cells
Intrathecal transplantation/ intravenous infusion
BDNF, GDNF, NGF, VEGF, EPO
Reduced T-lymphocyte activation
Reduced microglial activation and cytokine secretion
Increased paracrine secretion of neurotrophic and angiogenic factors
Replacement of damaged resident cells
Immunomodulatory actions

Pharmacologic prenconditioning

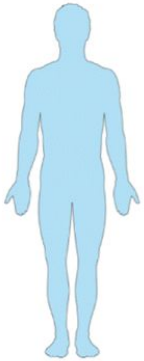
Hypoxic preconditioning



Hydrogel scaffold

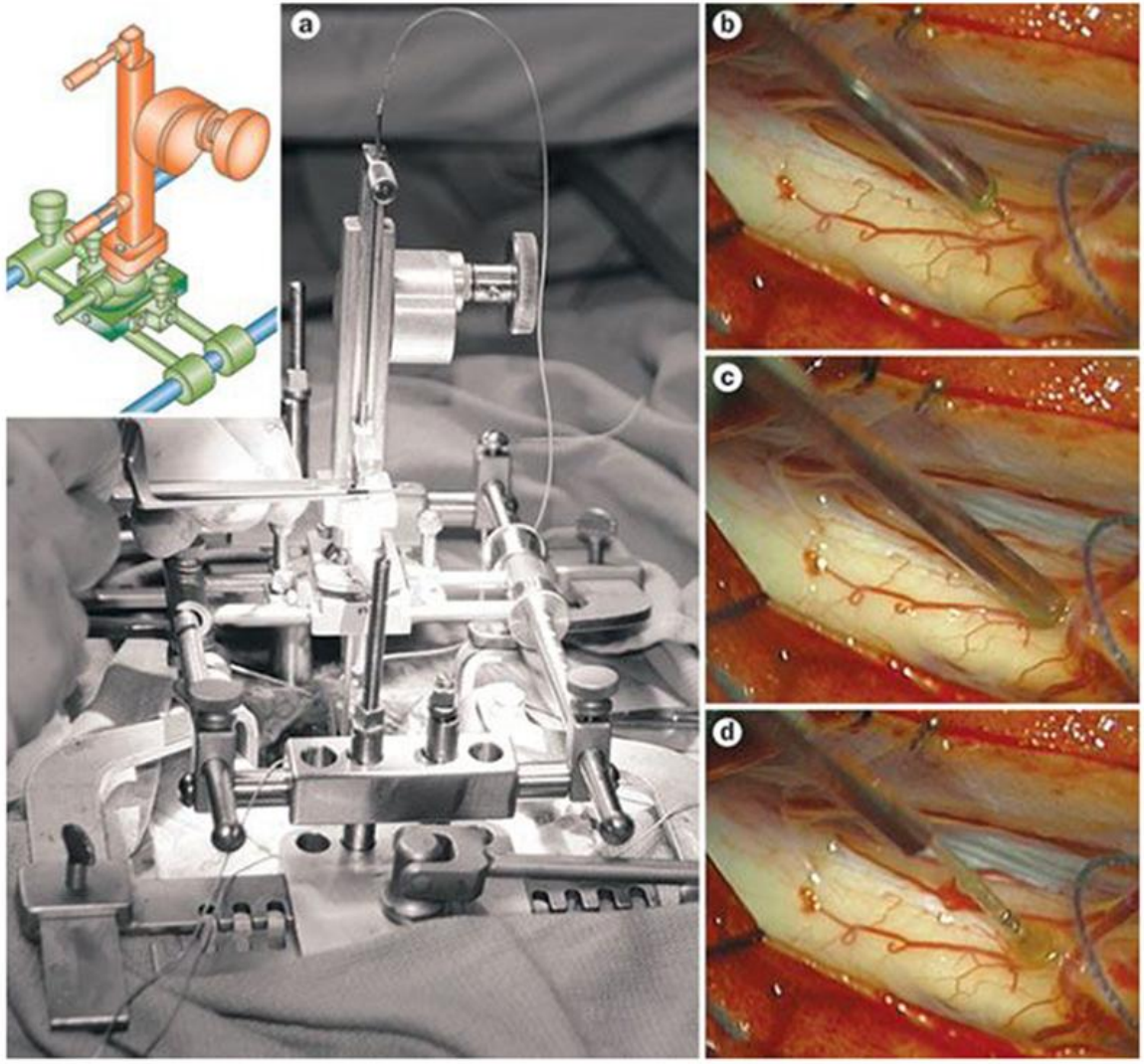


Genetic engineering



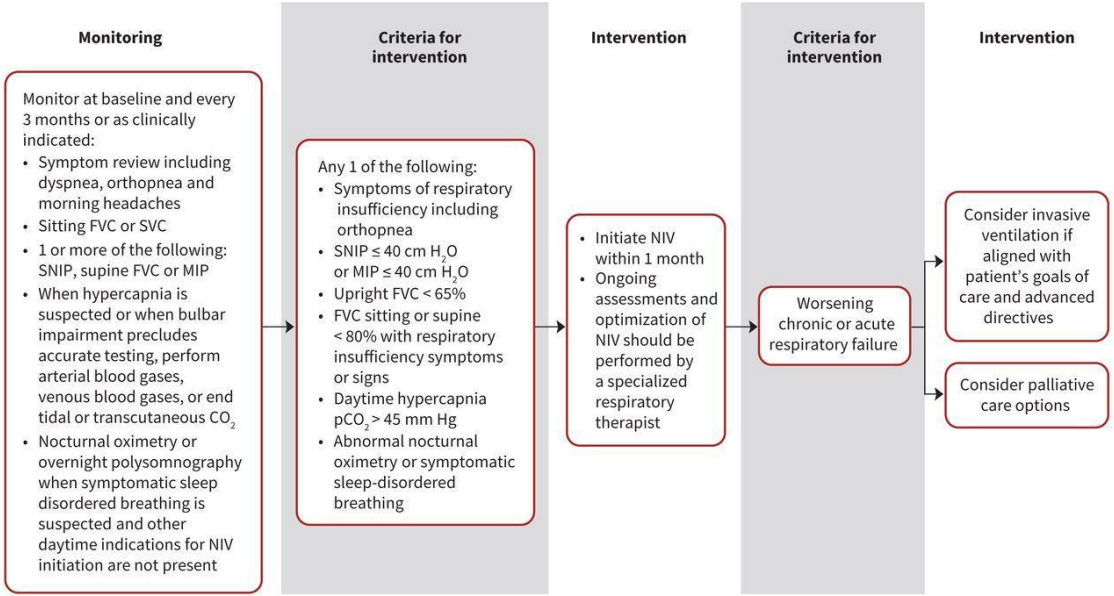
Transplantation of engineered cells

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

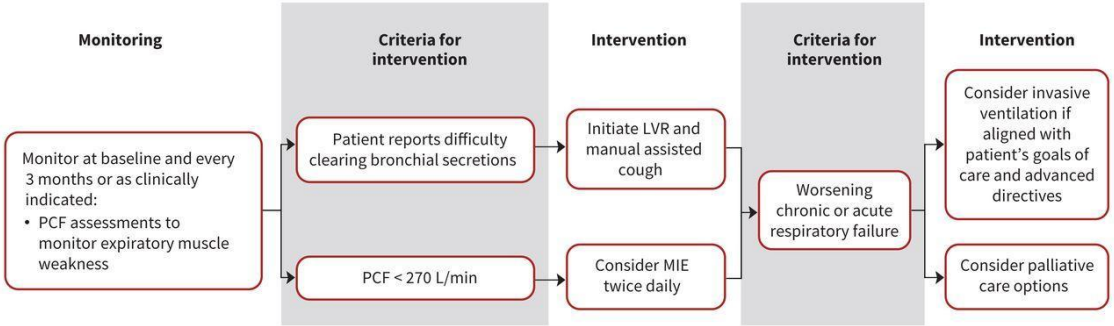

a
b
c
d

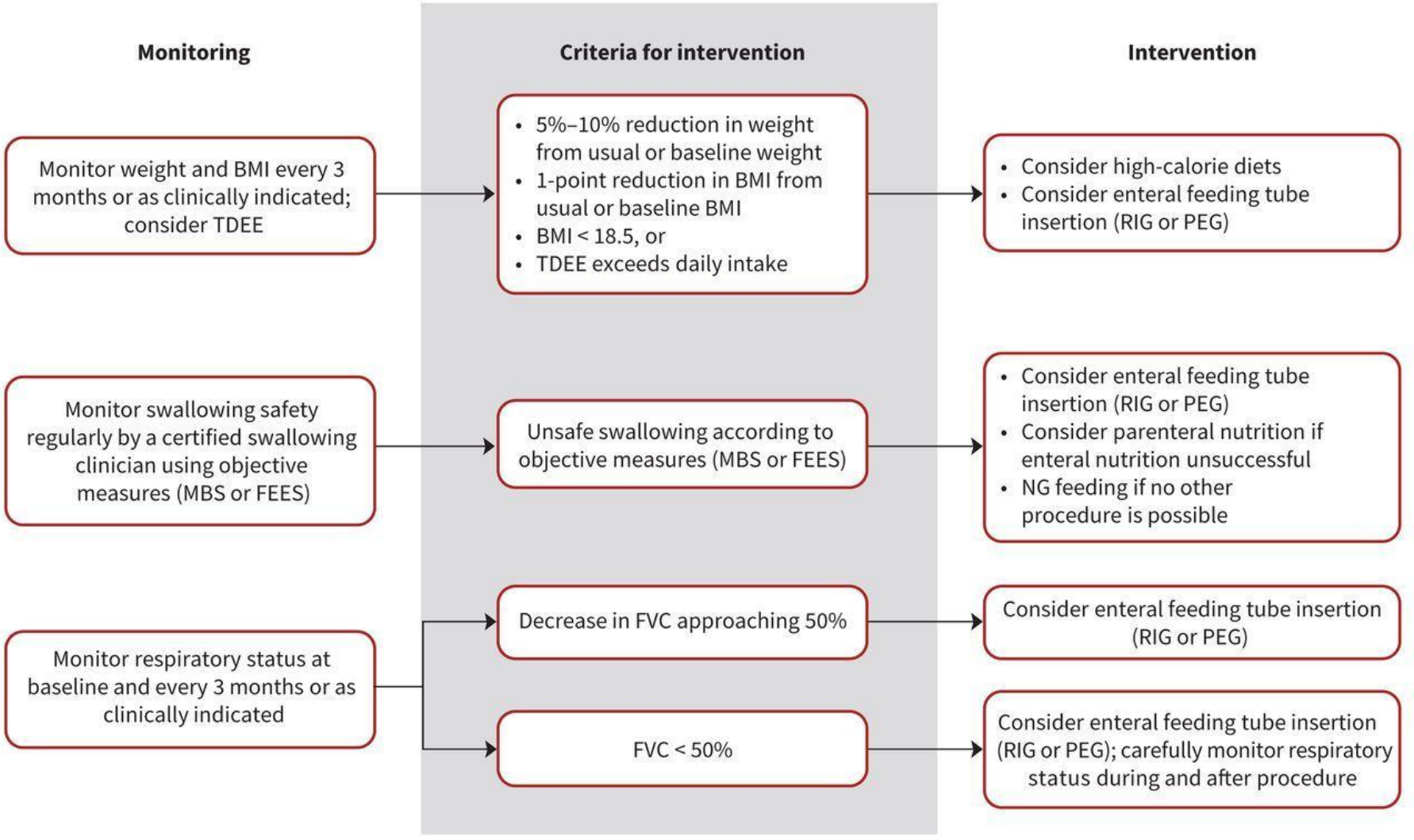
Cell source	Dose	Mode and site of delivery	Number of patients	Follow-up (months)	Adverse events	Refs.
Autologous bone marrow	1×10^6/kg × 2 doses	Lumbar intrathecal infusion	8 enrolled, 7 treated	12	Flu-like illness (62.5%), back pain (50%), headache (25%)	Oh et al. [44]
Autologous bone marrow	Phase 1/2: 1×10^6/kg Phase 2a: 1×10^6/kg, 1.5×10^6/kg, 2×10^6/kg	Lumbar intrathecal infusion ± 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 1×10^8 × 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
Criteria for intervention
Intervention
Monitor weight and BMI every 3 months or as clinically indicated; consider TDEE
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
Consider high-calorie diets
Consider enteral feeding tube insertion (RIG or PEG)
Monitor swallowing safety regularly by a certified swallowing clinician using objective measures (MBS or FEES)
Unsafe swallowing according to objective measures (MBS or FEES)
Consider enteral feeding tube insertion (RIG or PEG)
Consider parenteral nutrition if enteral nutrition unsuccessful
NG feeding if no other procedure is possible
Monitor respiratory status at baseline and every 3 months or as clinically indicated
Decrease in FVC approaching 50%
Consider enteral feeding tube insertion (RIG or PEG)
FVC < 50%
Consider enteral feeding tube insertion (RIG or PEG); carefully monitor respiratory status during and after procedure