

Wisconsin Department of Health Services



Wisconsin Public Psychiatry Network Teleconference (WPPNT)

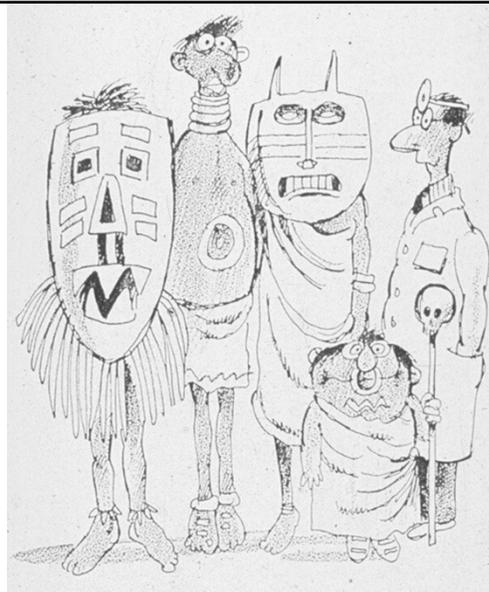
- This teleconference is brought to you by the Wisconsin Department of Health Services (DHS) Bureau of Prevention, Treatment and Recovery and the University of Wisconsin-Madison, Department of Psychiatry.
- The Department of Health Services makes no representations or warranty as to the accuracy, reliability, timeliness, quality, suitability or completeness of or results of the materials in this presentation. Use of information contained in this presentation may require express authority from a third party.

1

**Antipsychotic
Medications**

**The Good, the Bad and
the Ugly**

Ron Diamond
diamond@wisc.edu



**Four out of five doctors
recommend. . .²**

Evidence Based Practice (Modified from PORT Recommendations)

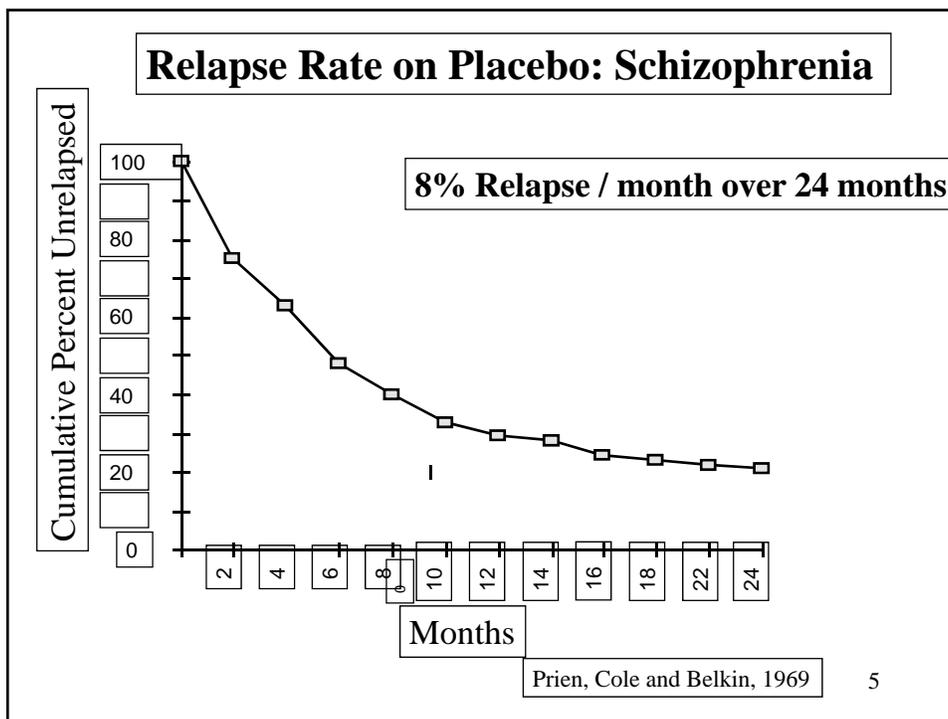
- **Family psycho-education**
- **ACT and Clubhouse psychosocial programs**
- **Integrated supported work programs**
- **Skill training**
- **Integrated Mental Health and AODA Treatment**
- **Cognitive Behavioral Therapy**
- **Cognitive Remediation**

Dixon L, et al. *Schizophr Bull.* 2010;36:48-70.3
Clubhouse not part of current PORT recommendations

Using medication as a tool to recovery

- **What does the consumer want this medication to do? What problem can it help to fix?**
- **What else has the consumer tried to also help deal with this problem?**
- **How would the consumer and others know if the medication was helping?**

Modified from Pat Deegan



Medication prices

Generic ziprasidone 80 mg # 60 tabs:	\$99.08
Brand name Geodon 80 mg # 60 tabs:	\$1106.52
Generic olanzapine 10 mg # 30	\$17.91
Brand name Zyprexa 10 mg #30	\$635.57
Generic quetiapine 100 mg # 100	\$16.32
Brand name Seroquel 100 mg # 100	\$740.98

**We prescribe medications so that our client's
"get better"...**

But what do we mean by "getting better"?

- **Feel better**
- **Decrease symptoms**
- **Increase function**
- **Increase stability/stay out of hospital**

- **Improve subjective sense of well-being**
- **Improve quality of life**

7

All medication has risks

- **Balance potential benefits Vs risks**
 - **What risks or benefits are most important**
 - **Question of values**
 - **Who gets to decide**

- **When is a risk "worth it"**
 - **What is the risk of NOT taking medication**

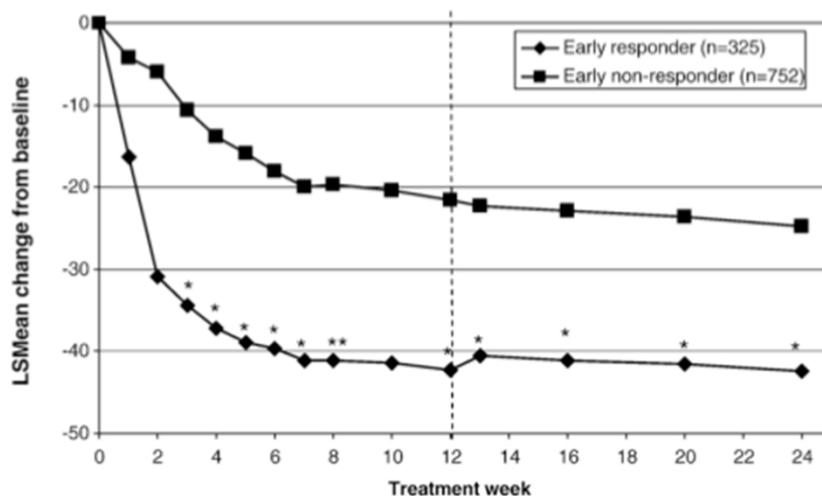
8

Need to develop “target list”

- What is the “target” of the medication: what behavior/feeling or experience do we hope will change?
 - What is the consumer hoping medication will do
 - What are others hoping medication will do
- Must be detailed, specific and concrete
- Based on observable behavior

9

Predicting Antipsychotic Response from Early Treatment Response



10

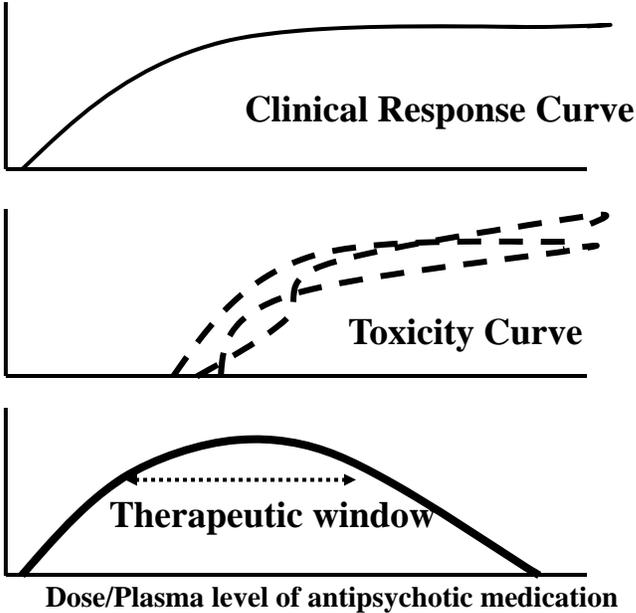
Kinon et al Schiz Res 102 (2008) 230-240

Treatment Adherence



11

Antipsychotic Dose-Response Curve



12

Antipsychotic Medications: Indications

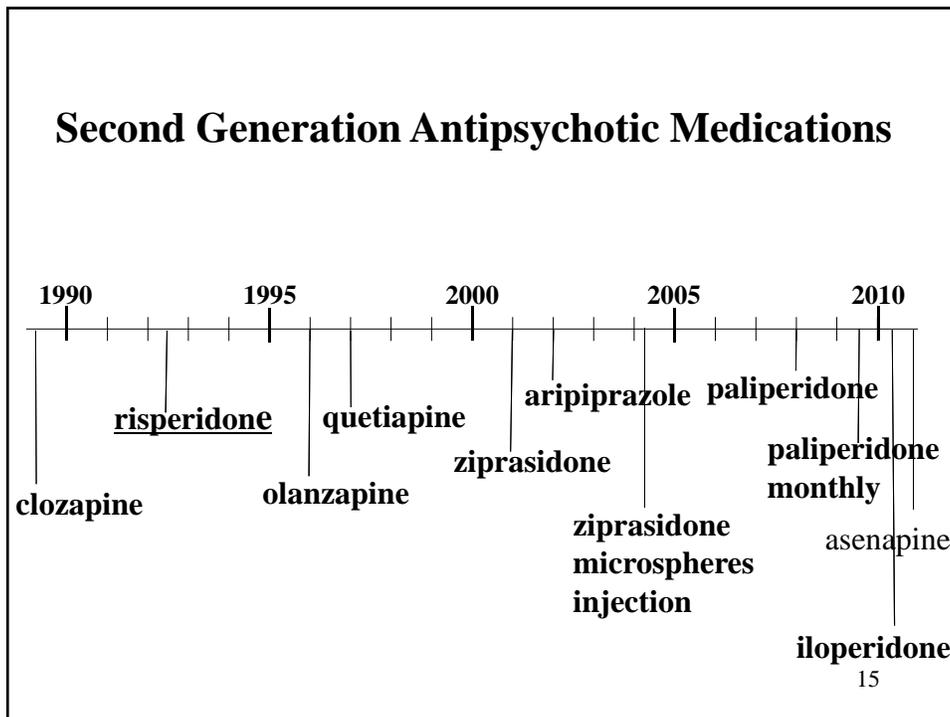
- Schizophrenia: + positive symptoms
 ? Negative symptoms
 ? Cognitive dysfunction
- Depression + psychotic depression
 ? Some (quetiapine)
- Bipolar disorder + anti-manic
- + mood stabilizer (some)
- OCD
- Autism related behaviors
- Aggression

13

Antipsychotic Medications: What do we really know?

- All are much more effective for positive sx than for negative sx or cognitive dysfunction
- Clozapine is more effective than any other, but has the most side effects and risks
- None of the others is clearly more effective than any other, but they are different and different people respond differentially
- The data on lifetime need is problematic and may be wrong, at least for some patients

14

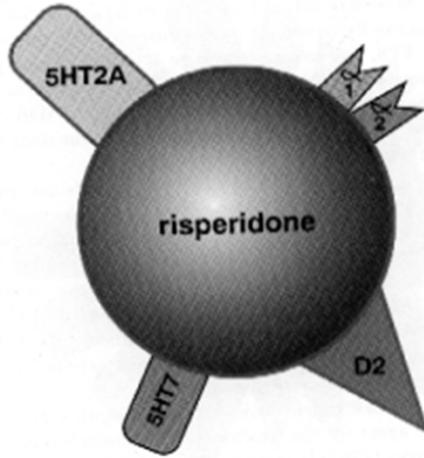


Clozapine

A diagram showing a central sphere labeled 'clozapine' with several receptor subtypes radiating from it. The receptors are labeled: 5HT2A, 5HT1A, M1, H1, 5HT2C, 5HT3, 5HT6, 5HT7, D4, D3, D1, and D2.

- **Other side effects**
 - Agranulocytosis
 - Heat Related Deaths
 - Heart related problems
 - Diabetes
 - Drooling
 - Seizures
- **Very effective**
 - positive and negative
 - good mood stabilizer
 - very low EPS
 - very low TD

Risperidone (Risperdal)



Adapted from Stahl
Essential Psychopharmacology

- Dose related EPS
- Less is better
- Prolactin Elevation
- Weight Gain
- Positive and negative efficacy
- Mood stabilizer
- Decreased TD
- Has a 2 week injection: Consta

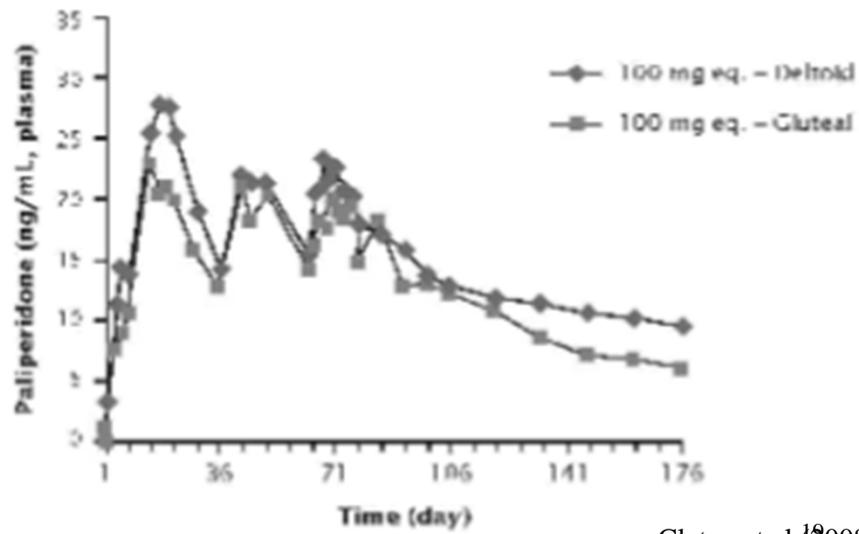
17

Paliperidone (Invega)

- Major metabolite of risperidone
- Similar prolactin elevation to risperidone
- Similar weight gain to risperidone
- Has a 4 week injection: Invega Sustenna

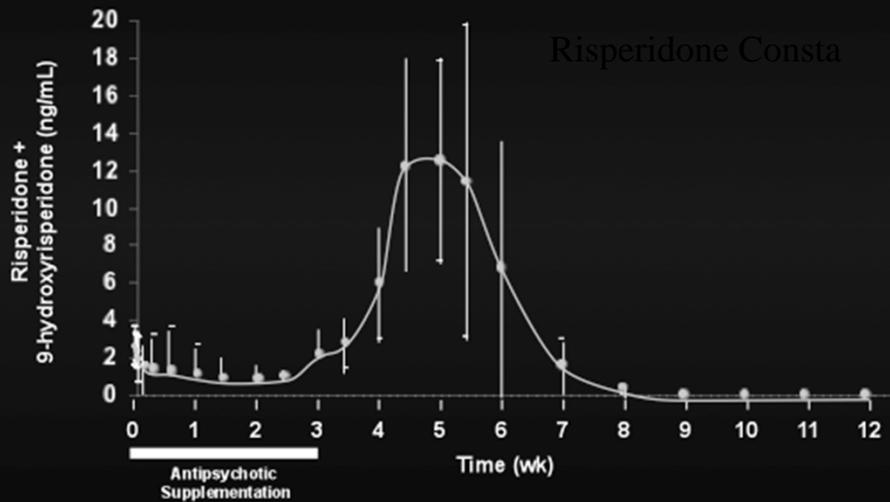
18

Figure 2. Median Paliperidone Palmitate Plasma Concentration vs. Time Profile



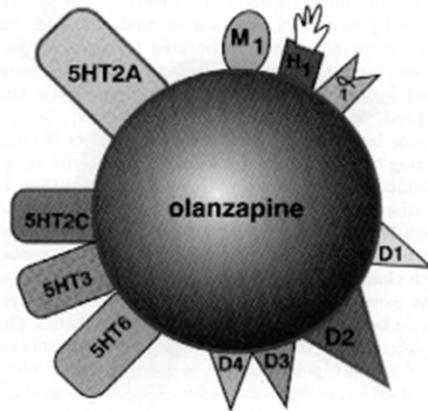
Cleton et al (2008)

Blood Levels Over Time After Single Dose*



*25 mg dose, n = 14.
Data on file, Janssen Pharmaceutica Products, L.P.

Olanzapine (Zyprexa)



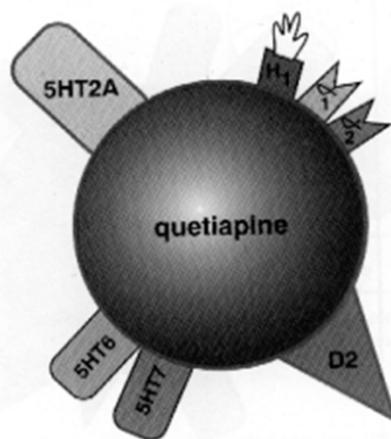
Adapted from Stahl
Essential Psychopharmacology

- **Big Weight Gain**
- **Diabetes risk**
- **Somewhat sedating**

- **Positive and negative efficacy**
- **Mood stabilizer**
- **Can be given in full dose in crisis situation**

21

Quetiapine (Seroquel)



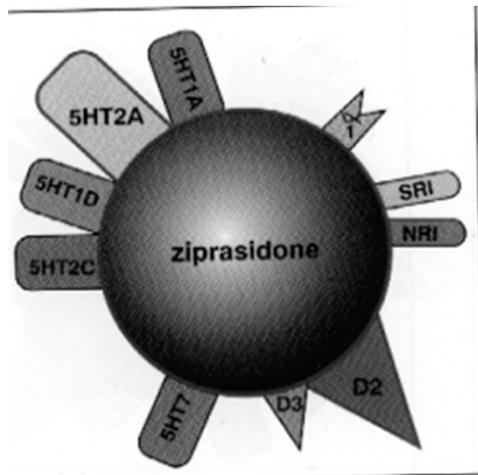
Adapted from Stahl
Essential Psychopharmacology

- **More is Better**
- **400 mg up to 1200 mg**
- **Very low EPS**
- **Very low TD risk**
- **Some weight gain**
- **Sedating**
- **Needs dose titration to decrease dizziness**

- **Low dose may be useful in people with borderline disorder**

22

Ziprasidone (Geodon)



Adapted from Stahl
Essential Psychopharmacology

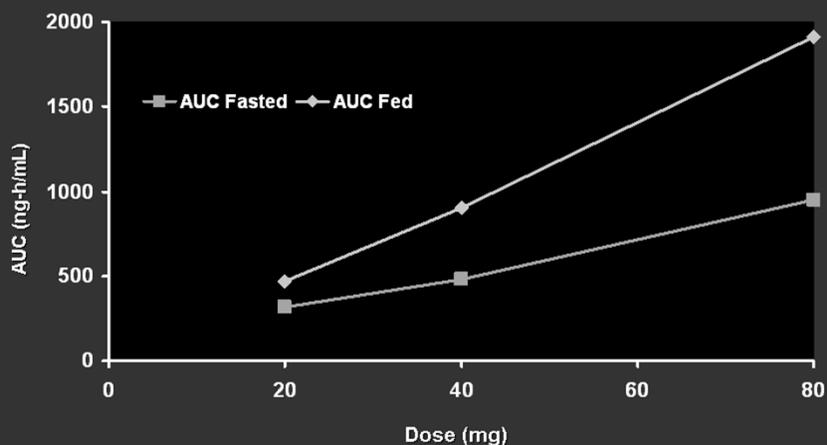
- **NO WEIGHT GAIN**
- **Very low diabetes risk**
- **Higher dose often better than low: rapid titration better than slow increase**
- **QTc prolongation**
- **Activating/agitating**
- **Antidepressant activity**

MUST BE TAKEN WITH FOOD!

23

Food Effect on Dose Dependence and Fasting PK: Study 006

Dose Ziprasidone With Food to Maximize Absorption



Data on file, Pfizer Inc.

24

Aripiprazole (Abilify)

- **Dopamine agonist/antagonist**
- **Some weight gain**
- **Some motor restlessness, dose related**
- **Not sedating**
- **Recently available as a generic**

**Highest Grossing Drug in U.S. 10/1/12-9/30/31
\$6,391,050,000**

25

Iloperidone (Fanapt)

- **“balanced” side effects**
- **Less weight gain than olanzapine, less EPS than risperidone, less sedation than quetiapine**
- **Must be titrated gradually to prevent dizziness**

Expensive branded product

26

Asenapine (Saphris)

- **Sublingual tablet (under the tongue)**
- **Less wt gain than olanzapine**
- **VERY LITTLE data published**
- **Side effects: reported in clinical trials**
 - **Akathisia**
 - **Oral hypothesia**
 - **Somnolence**
 - **Dizziness**
 - **Weight gain (some??)**

27

Lurasidone (Latuda) (FDA approved Oct 2010)

- **Similar to ziprasidone (Geodon)**
- **Weight neutral**
- **Some agitation**
- **Approved for bipolar depression**

- **\$2844.27 for # 120 of 40 mg tabs**

28

Brexpiprazole

- Partial d2 agonist
- Lower intrinsic d2 agonism affinity than aripiprazole, higher 5-HT1a/2a
- Similar to aripiprazole, but not about to become generic

29

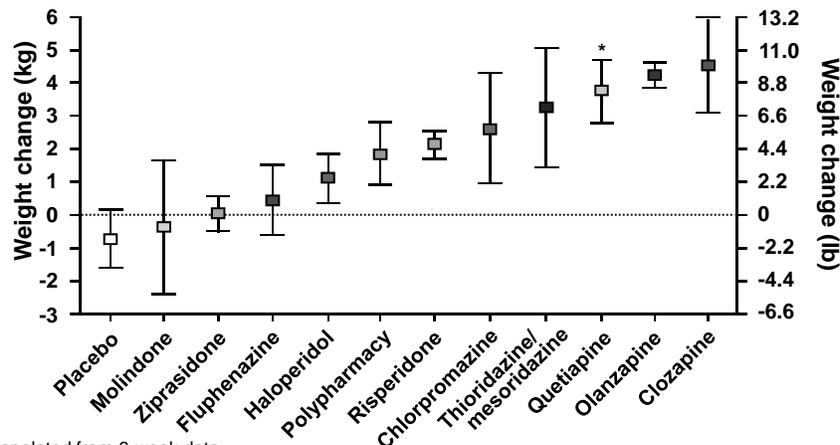
Side Effects of Antipsychotic Medications

	Clozapine	Risperidone	Olanzapine	Quetiapine	Ziprasidone	Aripiprazole	haloperidol
Weight gain	+++	++	+++	++	0	0	0
dyslipidemia	+++	+	+++	+	0	0	0
Diabetes	+++	++	+++	++	+	+	+
Sedation	+++	+	++	+++	±	±	±
EPS	±	++	+	±	+	+	++
↑ Prolactin	0	+++	+	0	0	0	+++

30

Mean Change in Weight With Antipsychotics

Estimated Weight Change at 10 Weeks on "Standard" Dose



*Extrapolated from 6-week data.
Allison et al. *Am J Psychiatry*. 1999;156:1686.

31

Long-acting injectable antipsychotics

1st Generation

- Fluphenazine deconoate [Prolixin Deconoate]
- Haloperidol deconoate [Haldol Deconoate]

2nd generation

- Risperidone [Risperdal Consta]
- Paliperidone palmitate [Sustenna-monthly]
- Olanzapine palmoate [Relprevv-monthly]
- Aripiprazole [Maintena-monthly]

32

Depot antipsychotic injection

After 180 days only

- 9.7% haldol deconotate**
- 5.4% still on fluphenazine dec**
- 2.6% still on Consta**

- More than 50% also took oral anipsychotic medication**

Olfson, Marcus and Ascher-Svanum Schiz Bull 2007:33(6)

33

The negative effects of medication

"Sure the drugs would do that (remove the auditory and visual hallucinations) but my ability to cognise was just totally impaired by drugs and once my ability to cognise was destroyed I would get deeper into psychosis. Yeah, deeper, less and less able to recognize myself".

Tooth, Kalyansundaram and Glover. Recovery from Schizophrenia: A consumer perspective 1998

34

Second Generation Antipsychotics: are they worth the cost?

- **CATIE**
- **CUTLESS**
- **Long-term VA study**

35

Recovery in Remitted First-Episode Psychosis at 7 Years of Follow-up of an Early Dose Reduction/Discontinuation or Maintenance Treatment Strategy: Wunderink et al 2013

- The DR patients experienced twice the recovery rate of the MT patients (40.4% vs 17.6%).
- Logistic regression showed an odds ratio of 3.49 (P =.01).
- Better DR recovery rates were related to higher functional remission rates in the DR group but were not related to symptomatic remission rates.

36

